NATURAL HISTORY OF HEPATOCELLULAR CARCINOMA IN CIRRHOTICS

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CERTIFICATE

This is to certify that this dissertation entitled **"NATURAL HISTORY OF HEPATOCELLULAR CARCINOMA IN CIRRHOTICS"** is a bonafide work done by DR. S.Raja during the study period 2008-2011 and is being submitted to The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirements for the award of DM Branch IV Medical Gastroenterology Degree.

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I declare that this dissertation entitled **"NATURAL HISTORY OF HEPATOCELLULAR CARCINOMA IN CIRRHOTICS"** has been done by me under the guidance and supervision of Prof. A.R.Venkateswaran, MD, DM. It is submitted in partial fulfillment of the requirements for the award of DM Gastroenterology degree by The Tamilnadu Dr. M.G.R. Medical University, Chennai. This has not been submitted by me for the award of any degree or diploma from any other University.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is a major health problem worldwide, due to its high incidence (approximately 600 000 new cases in 2008), and high rates of Mortality. It results in 598 000 deaths per year worldwide.(1) The incidence of HCC is increasing in almost all geographical areas and this neoplasm currently represents the third cause of cancer related death. In >90% of the cases, cirrhosis of any aetiology underlies HCC and the development of HCC constitutes their most frequent cause of death.

Overall, 75–80% of global HCC cases are due to hepatitis B virus (HBV) (50–55%) or hepatitis C virus (HCV) (25–30%). The identification that chronic liver disease is the relevant risk factor for this tumor, has made surveillance campaigns aimed at early detection of HCC possible and surveillance is now universally recognized to be the practical approach for improving treatment of HCC patients.

From a global perspective, the two most important risk factors for HCC are chronic hepatitis B and C infection. The geographic distribution patterns of HCC and HBV almost coincide with each other. Recent studies demonstrated that the Taiwanese mass vaccination program against HBV has significantly reduced the carrier rate of HBsAg in

children and adolescents and, as anticipated, the incidence of childhood HCC. A substantial decrease in HCC incidence in adults may be observed in 3–4 decades.

In contrast, the incidence of HCC has risen in the past 10–20 years in several developed countries such as the United States, Japan, England, and France where HBV is not endemic. Recent review suggested that a cohort effect related to HCV infection may likely contribute to the increasing disease burden in these countries. In India, the mean incidence of HCC in four population-based registries is 2.77% for males and 1.38% for females. The prevalence of HCC in India varies from 0.2% to 1.6%. The characteristics of patients with HCC are influenced by the etiology and the status of the underlying liver disease. The understanding of its natural history may influence the prognosis and choice of treatment.

Most of the published literatures were retrospective studies and moreover limited number of studies available for South Indian population.

Hence we have undertaken this **prospective study** to analyze the natural history of HCC, especially with regard to patients with cirrhosis.

AIMS & OBJECTIVE OF THE STUDY

To prospectively study the natural history of Hepatocellular Carcinoma in patients with cirrhotic background in a tertiary care hospital.

REVIEW OF LITERATURE

Hepatocellular carcinoma (HCC) is the third most common cause of cancer death in the world resulting in 598 000 deaths per year worldwide. Because of its poor prognosis, this number of deaths is almost the same as the number of cases being diagnosed each year (626 000) (1).

From a global perspective, the two most important risk factors for HCC are chronic hepatitis B and C infection.(2) The geographic distribution patterns of HCC and HBV almost coincide with each other. The characteristics of patients with HCC are influenced by the etiology and the status of the underlying liver disease. The understanding of its natural history may influence the prognosis and choice of treatment of HCC represents more than 5% of all cancers in the world. With the significant increase in the number of patients who have HCC, early detection and treatment of this tumor are vital to improve outcomes.

Epidemiology

Worldwide Distribution

Liver cancer incidence rate varies widely from 52.1 per 100 000 in China to 5.1 per 100 000 in Northern Europe. Developing countries contribute more than 80% of cases with China alone accounting for 55%

(1). More than 80% of HCC cases occur in either sub-Saharan Africa or in Eastern Asia. China alone accounts for more than 50% of the world's cases (men, 35.2/100,000; women, 13.3/100,000).(62) North and South America, and Northern Europe found to have low incidence (<5.0/100,000) of liver cancer among most populations. United Kingdom (male, 2.2/100,000; female, 1.1/100,000) and Australia (male, 3.6/100,000; female, 1.0/100,000) also noted low tumor burden. Other areas, with high incidences are sub-Saharan Africa, eastern and southeastern Asia, and Melanesia.(16)

It is believed that effective HBV vaccination programmes and the better control of aflatoxin exposure in the high HCC incidence areas are contributing to the decreased HCC incidence while the increasing HCC incidence in some of the western countries is attributed to the increasing prevalence of hepatitis C virus (HCV) infection and immigration of people from countries with high endemicity for HBV infection. Neonatal vaccinations against hepatitis B virus (HBV) and shift the staple diet from corn to rice (limit the exposure to aflatoxin B1) lowered the incidence of HCC in Asian countries.

Race/Ethnicity

HCC incidence rates vary greatly among different populations living in the same region. In United States, HCC rates are 2 times higher in Asians than in African Americans, whose rates are 2 times higher than those in whites. The reason for this ethnic variability includes differences in the prevalence and acquisition time of major risk factors for liver disease and HCC. (17)

Age & Sex

There is no evidence that advanced age per se is associated with greater cancer aggressiveness. Confounding factors such as shorter life expectancy, higher prevalence of co-morbidities and less 'aggressive' therapeutic management could explain the negative impact of age on prognosis. In fact, the adverse effect of age disappeared when patients were segregated according to the treatment received . In almost all, males have higher liver cancer rates than females, with male: female ratios usually averaging between 2:1 and 4:1. The reasons for higher rates of liver cancer in males may relate to sex-specific differences in exposure to risk factors. Men are more likely to be infected with HBV and HCV, consume alcohol, smoke cigarettes, and have increased iron stores.

Age

The global age distribution of HCC varies by region, incidence rate, sex, and by etiology. Male sex is an established risk factor for HCC in patients with chronic liver diseases(9) , whereas gender influence on HCC progression and prognosis remains controversial. Androgen hormones have been claimed as responsible for the greater cancer risk and grim prognosis . Among the low-risk populations (United States, Canada, and United Kingdom), HCC commonly occurs in persons aged 75 and older.

A similar pattern is seen among most high-risk Asian populations (Hong Kong and Shanghai). In contrast, male rates in high-risk African populations tend to peak between ages 60 and 65, whereas female rates peak between 65 and 70. These variable age specific patterns likely are related to differences in the dominant hepatitis virus in the population, the age at viral infection, and the existence of other risk factors. Although most HCV infections acquired in adulthood, but most HBV carriers became infected at very young ages.

DIFFERENT HCC PATTERNS

HCCs in South Africa are mostly large sized and poorly differentiated with relatively healthy surrounding liver tissues. On the contrary, HCCs in non-African countries are relatively smaller in size and more differentiated with a background of cirrhotic liver. This can be the result of the difference in etiologies. Aflatoxin B1, a mycotoxin produced by Aspergillus species-- major carcinogenic factor in the South African population. Chronic hepatitis and the resultant cirrhosis are important risk factors in non-Africans. The distinct fibrolamellar type of HCC almost exclusively found in young Caucasian patients may be due to ethnic factor.

HCC in Asia

In China and Taiwan, almost one-fifth of the populations are carriers of HBV, and the majority of persons with HCC are HBsAg-positive(60). In contrast to the rest of Asia, cases of HCC in Japan are mainly related to HCV infection, and its incidence is rising but on a larger scale. The reasons underlying this difference are likely related to the wide transmission of HCV to young people in Japan from contaminated blood and needles after the Second World War. In Japanese patients with

chronic viral hepatitis, the progression to HCC occurs at an accelerated rate in HCV infection compared with HBV infection. (58,59)

HCC in India

Most Asian countries are in intermediate or high incidence zones of HCC. In India, the mean incidence of HCC in four population-based registries is 2.77% for males and 1.38% for females. HCC accounted for 1.9% of the 24,975 cases of cancers recorded at 6 registries put together; the proportion ranging from 1.1% (94/8763) in Delhi to 5.3% (10/187) in Barshi rural registry. The prevalence of HCC in India varies from 0.2% to 1.6%.(61) In India HBV is the main etiological factor associated with HCC. However, in India, most of the patients in clinical practice present at an advanced stage ruling out curative treatment in most cases. A prospective study by Paul et al revealed the estimated incidence of HCC among cirrhotic patients was 1.6% per year.(66)

Risk Factors and Pathogenesis of HCC

Hepatocellular carcinoma is multi factorial in etiology and complex in pathogenesis. The main established risk factors for HCC development are chronic viral hepatitis B and C infection and aflatoxin B1.(76). Liver cirrhosis per se may also lead to HCC development. Hepatitis C infection

probably causes HCC through the pathway of cirrhosis. Alcoholic liver disease, autoimmune liver diseases, primary hemochromatosis and Wilson's disease are also associated with the development of HCC. Overall, hepatitis B and C infections are causally associated with over 80% of HCC in the world.

Worldwide, 400 million people infected with chronic hepatitis B, 75% of whom are Asians. The natural history of chronic hepatitis B infection in Asian and African countries is different from that in the western world. In Asia and Africa, the majority of the people acquire the infection during the perinatal period or during very early childhood. There is characteristically prolonged immune tolerance phase in the first few decades of life. The lifetime risk of HCC in infected men is estimated to be 10% to 25% while the risk in women is somewhat lower

Case-control studies - chronic HBV carriers have more than 100-fold increased risk of HCC compared with non- infected individuals. Furthermore, the risk of HCC development is related to the disease status of chronic hepatitis B infection. For example, the estimated annual risk of HCC in chronic carriers is 0.26% to 0.6%. The risk increases to 1% in patients with active hepatitis . It further increases to 2% to 3% in cirrhotic patients. Studies in Taiwan showed that genotype C chronic hepatitis B

infection has a more aggressive progression than genotype B in HBeAg positive patients. Core promoter mutations (T1762. A1764) are also found to be related to a more progressive disease . In the majority of HCC cases (70% to 90%), there is underlying liver cirrhosis. However, HBV, being an oncogenic virus, can cause HCC in the absence of cirrhosis through the pathway of integration into the human genome.

Major Risk Factors (67)

- **Chronic hepatitis B virus infection**
- **Chronic hepatitis C virus infection**
- **Cirrhosis**
- **Dietary exposure to aflatoxin B1**

Minor Risk Factors

- **Oral contraceptive steroids**
- **Cigarette smoking**
- **Dietary iron overload in persons of black African ancestry**
- **Hereditary hemochromatosis**

- **Wilson disease**
- **α1-Antitrypsin deficiency**
- **Type 1 hereditary tyrosinemia**
- **Type 1 and type 2 glycogen storage disease**
- **Membranous obstruction of the inferior vena cava**

Hepatitis B Virus

In the meta-analysis of 32 case control studies by McMahon et al.,(45) concomitant infection with HBV and HCV was associated with an odds ratio of 165 (95% CI, 81 to 374) as compared with an odds ratio of 17 with HCV positivity alone and an odds ratio of 23 with HBV positivity alone, thus, suggesting a synergism between the 2 infections. Carcinogenesis of HCC is a multi-step process involving a number of different genetic alterations that ultimately lead to malignant transformation of the hepatocyte. It is postulated that HBV infection causes HCC via direct and indirect pathways.

Continuous hepatocyte injury and regeneration in cirrhosis of the liver leads to increased liver cell turn over and hence accumulation of critical mutations in the host genome resulting in genetic alterations,

such as chromosomal rearrangements as well as activation of cellular oncogenes or inactivation of tumor suppressor genes. However a higher rate of chromosomal abnormalities is found in HBV-related HCC than those linked to other risk factors (45). The HBsAg positivity in Indian HCC patients varies from 36% to 74%. 10, 11.

India in an intermediate endemic zone for HBV has low incidence of HCC unlike other Asian countries. The relative risk of developing HCC in Indian patients with chronic HbsAg infection estimated to be 7.8 - studies.

HBV belongs to the group of oncogenic viruses known as hepadna virus. It is able to integrate its DNA into the genome of the infected cell. Integrated HBV sequences have been observed in established hepatoma cell lines and in about 80% of human HBV related HCCs . It is postulated, that the HBV DNA integration may confer a selective growth advantage on target cells and leads to the onset of tumor progression. The integration sites are frequently detected in cellular genes involving cell signaling or growth control. Host chromosomal instability is also enhanced by HBV DNA integration. Large inverted duplications, deletions, amplification, chromosomal translocation have all been observed to be associated with HBV integration(46,47). Regulatory

proteins HBx and the PreS2 activators can exert a tumor promoter-like function, resulting in positive selection of cells producing a functional regulatory protein. Hepatitis B vaccination - recognized as the most effective measure to prevent HBV infection and HBV-associated complications, including HCC. The first evidence came from Taiwanese study - HCC is preventable via effective vaccination. The average incidence of HCC declined from 0.7 (1982 to 1986) to 0.36 (1990 to 1994) per 100,000 children(36,41,47). And there was a similar decline in the mortality associated with HCC. HBV-related HCC is predominant in male, with a male to female ratio of 5–7:1. This is attributed to the elevated androgen level and the enhanced androgen receptor (AR)-mediated activity in the host. HBx is a noncellular positive coregulator for androgen receptors makes males vulnerable to HBV infection & subsequent development of cancer. HBx protein may play a significant role in inducing the expression of angiopoietin-2; contribute to pathological angiogenesis and Hepatocellular carcinoma progression.

Hepatitis C Virus

Several lines of evidence indicate a strong causal association between HCV and HCC. Markers of HCV infection are found in a variable proportion of HCC cases in Europe with an increasing gradient

from North to South (44); for example,44% to 66% in Italy,27% to 58% in France, 60% to75% in Spain,and in 80% to 90% of HCC cases in Japan. Moreover, the age-standardized death rates owing to HCC(49) in several European countries are significantly correlated with the seroprevalence of HCV in the general population.

Of 1,429 patients assumed to have been tested, 384 (27%) were positive for HCV.11-15. Higher proportion of patients with HCC might have had HCV detected by polymerase chain reaction testing of liver tissue and/or serum, even if antibody to HCV (anti-HCV) was not detectable, particularly if I generation tests were used.

HCV increases the risk for HCC probably by promoting fibrosis and cirrhosis; virtually all HCV-related HCC cases occur among patients with cirrhosis. With the exception of areas in the world where hepatitis B is endemic, it is uncommon to find HCC in the absence of cirrhosis.

The duration of HCV infection is especially relevant to HCC development, with most cases of HCC occurring after 25 to 30 years of chronic infection .This long period probably reflects the time needed for the development of cirrhosis. HCV infection is a more important factor than HBV in the development of HCC in western countries.

Markers of HCV infection are found in a higher proportion of HCC patients than that in most of the Asian countries; ranging from 44% to 66% in Italy, 27% to 58% in France, 60% to 75% in Spain, Japan, unlike other Asian countries also has a high proportion of HCC caused by HCV infection accounting for 80% to 90% of all the cases. HCC risk increases to 17-fold in HCV-infected patients compared with HCV-negative subjects. The risk of HCC occurrence is different among all HCV patients. It is a function of the degree of liver fibrosis and the time of acquisition of the infection. The risk for cirrhotic HCV patients (F4) was the highest with 5.8% per year, compared to those who had less fibrosis (F1-3, 0.5% to 2.6%) .Because of the absence of reverse transcription activity of the HCV RNA virus, its viral genome unlike HBV is not able to integrate into the genome of the infected cell. Therefore, HCV causes HCC via an indirect pathway by causing chronic inflammation, cell death, proliferation and cirrhosis.(81) HCV-related HCCs are almost exclusively found in patients with cirrhosis. Studies raising the possibility that HCV - operate through other pathways in promoting malignant transformation of hepatocytes.

Co-infection with HIV

Studies indicated that HCV/HIV coinfection is associated with an increased risk for cirrhosis as compared with patients with HIV who are not coinfected, (54).

Two studies in HCV-infected patients with hemophilia - nonsignificant trend toward lower rates of HCC in patients with coinfection as compared with those infected only with HCV.(75)

Patients co-infected with HIV and either hepatitis B or hepatitis C may have more rapidly progressive liver disease and when they reach cirrhosis they are also at increased risk of HCC. The **MORTAVIC** study indicated that HCC was responsible for 25% of all liver deaths in the post-HAART era.(74)

Treated chronic HBV and HCV infections

There is no convincing evidence that interferon treatment of chronic hepatitis B reduces the incidence of HCC. sA meta-analysis conducted in patients with chronic HCV infection concluded that the benefit with interferon treatment was mainly seen in those who achieved sustained virological response, however the effect was small. The steps required to initiate the carcinogenic pathway probably occur many years

before the disease becomes inactive, and so the threat of HCC remains even if fibrosis decreases. Regressed fibrosis is not a rationale to withhold surveillance.29

Cirrhosis and HCC

Most often HCC occurs within an established background of chronic liver disease and cirrhosis (70%–90% of all detected HCC cases)(31). Major causes of cirrhosis in patients with HCC include hepatitis B, hepatitis C, alcoholic liver disease, and possibly nonalcoholic steatohepatitis. Less common causes include hereditary hemochromatosis, alpha-1 antitrypsin deficiency, autoimmune hepatitis, and some porphyrias. Cirrhosis is macro nodular and is attributed to chronic HBV infection in Chinese and African populations, whereas in others, cirrhosis is commonly mixed macro nodular and micro nodular. Micro nodular cirrhosis may results from chronic HCV infection, alcohol abuse, or both. Cirrhosis contributes to hepatocarcinogenesis mainly by acting as a potent tumor promoter. Male sex, age, and duration of cirrhosis are the major risk factors for Hepatocellular carcinoma in cirrhotic patients.

Alcohol Consumption

HCV infection and alcohol induced liver disease are both risk factors for HCC, although the former seems to be the more predominant risk factor. Presumably, they operate together to increase the risk for HCC by more actively promoting cirrhosis. Studies that compared development of HCC among HCV infected patients with the development of HCC persons with non-cirrhotic liver disease or controls have found only a modest effect of alcohol (mostly heavy alcohol use of more than 50 g/d). For example, a recent study by Donato et al. reported that among alcohol drinkers, the risk for HCC increased in a linear fashion with a daily intake greater than 60 g, and that the presence of HCV had a positive synergistic action with an additional 2-fold increase in the risk over that caused by alcohol alone. In addition, the proportion of patients testing positive for anti-HCV increased significantly among heavy drinkers with severe liver disease (cirrhosis or HCC) as compared with those with mild or no disease.

The "Classic Triad"

In clinical practice, HCC often present with the triad of right upper quadrant abdominal pain, weight loss, and hepatomegaly.(68) Patients with these symptoms at presentation usually have a tumor larger than 6 cm. The pain is a dull continuous ache that intensifies late in the course of

the illness due to involvement of Glisson's capsule. The pain may be referred to the shoulder. Firm, often massive, nodular hepatomegaly is an invariable feature of symptomatic HCC. An arterial vascular bruit due to increased vascularity may be a useful diagnostic pointer. Observed in 25% of cases, occurs in systole, rough in character, and is not affected by changing the position.

Tumor Rupture: "Hemoperitoneum"

Spontaneous rupture is a rare and catastrophic complication of HCC that may occur if a large vascular tumor on the periphery of the liver. The clinical presentation is that of severe abdominal pain, vascular collapse, and signs of peritoneal irritation. Hemoperitoneum is a frequent event late in the course of the disease, it is a presenting feature in less than 5% of cases. The diagnosis is established by paracentesis, which reveals bloodstained fluid. Angiography and embolization of the bleeding vessel can be an effective method for managing this life threatening complication.

Extra hepatic Endocrine and Paraneoplastic Syndromes

These systemic sequelae result from synthesis and secretion of biologically active substances by the tumor. Less than 5% of patients

results in hypoglycemia. Type A hypoglycemia is a milder form of glycopenia that occurs in the terminal stages of Hepatocellular carcinoma due to increased demands for glucose by a large rapidly growing tumor. Type B hypoglycemia is believed to result from the defective processing by malignant hepatocytes of the precursor to insulin-like growth factor II (pro-IGF-II).

Polycythemia (<10% of patient) is caused by synthesis of erythropoietin by the tumor. Patients with sclerosing type of HCC may present with hypercalcemia in the absence of osteolytic metastases. Arterial hypertension complicating HCC is the consequence of ectopic synthesis of angiotensinogen by malignant hepatocytes. Feminization results from the tumor's conversion of circulating dehydroepiandrosterone to estrone. Hypercholesterolemia is the result of de novo synthesis of cholesterol by the tumor. Watery diarrhea is occasionally severe and intractable, probably is related to secretion of peptides that promote intestinal secretion such as vasoactive intestinal peptide, gastrin, and prostaglandins. Cutaneous manifestations are not specific for the diagnosis of HCC. It includes dermatomyositis, pemphigus foliaceus, sign of Leser-Trelat, pityriasis rotunda, and porphyria cutanea tarda.

Paraneoplastic Syndromes Associated With HCC(77)

- Hypoglycemia
- Polycythemia (erythrocytosis)
- Hypercalcemia
- Sexual changes: isosexual precocity, gynecomastia, feminization
- Systemic arterial hypertension
- Watery diarrhea syndrome
- Carcinoid syndrome
- Osteoporosis
- Hypertrophic osteoarthropathy
- Thyrotoxicosis
- Hypercholesterolemia
- Thrombophlebitis migrans
- Polymyositis Neuropathy
- Cutaneous manifestations: pityriasis rotunda, Leser-Trelat sign, dermatomyositis,
- Pemphigus foliaceus, porphyria
- cutanea tarda

Serum Alfa-fetoprotein

First one described α-fetoprotein (AFP). is more helpful. AFP is a glycoprotein that normally is produced during gestation by the fetal liver and yolk sac. Normally, it is present in high concentration in the fetal serum. AFP is elevated in 60– 70% of patients with HCC. The normal range of this serum marker is 0–10 ng/mL, and levels more than 400 ng/mL are diagnostic of HCC(39). False-positive results may be caused by acute and chronic benign hepatic diseases with a high necro inflammatory activity, germ cell tumors, or pregnancy. The sensitivity, specificity, and positive predictive value of AFP in three well-performed screening studies for HCC ranged from 39 to 64%, 76 to 91%, and 9 to 32%, respectively**.**

Alfa-fetoprotein (AFP) is a fetal glycoprotein whose circulating level quickly decreases after birth to 10 ng/ml. About 30–70% of HCCs produce AFP causing an elevation in plasma levels; in 50% of these cases, AFP levels are directly proportional to cancer size . Moreover, AFP levels tend to parallel the tumor volume doubling time . An elevated AFP is an established predictor of recurrence after resection and reflects a poor prognosis . A fucosylated variant of AFP, the so-called Lens culinaris agglutinin A-reactive AFP, correlates with cancer infiltrative

growth, vascular invasion, low-grade differentiation, multiple cancer recurrence and poor prognosis..

AFP production is age-related. Younger patients are more likely to have raised levels and to attain very high concentrations. Because of both false-positive and false-negative results, serum AFP falls short of being an ideal tumor marker.

Several attempts made to improve the HCC specificity of AFP by measuring particular glycoforms of the protein. These isoforms have differential affinities for lectins such as Lens culinaris agglutinin and concanavalin A. Lens culinaris-reactive AFP, also known as AFP-L3, may be superior to total AFP as a marker of HCC.

Diagnostic Imaging

Once a screening test is abnormal or there is a clinical suspicion that a patient may have HCC, imaging is very important for the diagnosis and staging of this tumor.

Ultrasonography

Ultrasonography often used as a screening method for high-risk patients and is repeated at frequent intervals. A small HCC may be

hypoechoic, hyperechoic, or isoechoic on USG The ultrasonographic appearance is influenced by the presence of fat, calcium, and necrosis(80). Advantages of USG include safety, availability, and cost effectiveness, though it is operator dependent. Approximately two thirds of symptomatic HCC are uniformly hyperechoic, whereas the remainder is partly hyperechoic and partly hypoechoic. Ultrasonography with Doppler technology is useful for assessing the patency of the inferior vena cava, portal vein and its larger branches, hepatic veins, and biliary tree.

CT scan and MRI

The most reliable diagnostic tests are triple-phase helical CT and triple-phase dynamic contrast enhanced magnetic resonance imaging (MRI)(37). HCC derives its blood supply predominantly from the hepatic artery, whereas the remainder of the nontumorous liver receives both arterial and portal blood. The hallmark of HCC during CT scan or MRI is the presence of arterial enhancement followed by delayed hypointensity of the tumor in the portal venous and delayed phases .The presence of arterial enhancement followed by washout has a sensitivity and specificity of 90% and 95%, respectively. However, 71% of patients with HCC will have arterial enhancement and whereas the rest do not have

these features and, therefore, will require liver biopsy for the diagnosis of HCC.

Studies show that MRI is slightly better in the characterization and diagnosis of HCC when compared with CT scan(106). The performance of CT and MRI is affected by the size of the lesions. Tumors larger than 2 cm, MRI are reported to have accuracy >90%; however, in tumors smaller than 2 cm, this level is reduced to 33%.

Treatment for HCC

Liver transplantation

Liver transplantation is done to replace the diseased liver with a cadaveric liver or a living donor graft. OLT is the best treatment option for HCC because it eliminates the tumor together with the entire diseased liver, thereby eliminating the risk for development of de novo HCC. In the early 1990s the results of OLT for HCC were dismal, with 1-year survival rates of 10% to 70% and 3-year recurrence rates up to 69%(24). Mazzaferro and colleagues published a landmark paper on OLT for HCC. When OLT was restricted to patients who had a single tumor of 5 cm or less and no more than three tumors, each less than 3 cm in diameter, the 4- year survival rate was 75%, and the recurrence-free survival rate was 83%(15). For the 35 patients (73%) who met the predefined criteria, the

overall and recurrence-free survival rates were 85% and 92%, respectively. In the 13 patients (27%) who had tumors exceeding the criteria, the overall survival rate was 50%, and the recurrence-free survival rate was 59%.(28)

The United Network for Organ Sharing (UNOS) has adopted these criteria. The number of available donors worldwide and therefore only a finite number of transplantations for HCC will be performed. In addition, waiting time for liver transplants is increasing worldwide, from 6 months to more than a year. Therefore, some patients will not be able to proceed to OLT because of tumor progression or deterioration in medical condition. In the United States, patients who have HCC receive higher-ranking scores to shorten their waiting time and to prioritize them.

During 1996–2001 the rate had improved to 61.1%, likely related to adoption of the Milan criteria at US transplantation centers. Expanded Shanghai criteria in China resulted in overall survival and disease-free survival rates similar to the Milan criteria. Studies from the late 2000 obtained higher survival rates ranging from 67% to 91%. If the liver tumor has metastasized, the immunosuppressant post-transplant drugs decrease the chance of survival. Considering this objective risk in conjunction with the potentially high rate of survival, some recent studies

conclude that: "LTx can be a curative approach for patients with advanced HCC without extrahepatic metastasis"[51,52] For those reasons, and others, it is considered nowadays that patient selection is a major key for success.[52]

Receptor tyrosine kinase

A new receptor tyrosine kinase inhibitor, **Sorafenib** used in patients with advanced hepatocellular carcinoma. Sorafenib is a small molecule that inhibits tumor-cell proliferation and tumor angionesis(91,92). Spanish phase III shows- adds two months to the lifespan of late stage HCC patients with well preserved liver function. It also increases the rate of apoptosis in other tumor models. The results indicated that single-agent sorafenib might have a beneficial therapeutic effect.

Surgical resection

Surgical resection to remove a tumor together with surrounding liver tissue while preserving enough liver remnant for normal body function(18). This treatment offers the best prognosis for long-term survival, but unfortunately only 10-15% of patients are suitable for surgical resection. This is often due to extensive disease or poor liver

function. Resection in cirrhotic patients carries high morbidity and mortality(22). The expected liver remnant should be more than 25% of the total size for a non-cirrhotic liver, while that should be more than 40% of the total size for a cirrhotic liver. The overall recurrent rate after resection is 50-60%.(23)

Percutaneous ethanol injection

Percutaneous ethanol injection (PEI) well tolerated, high RR in small (<3 cm) solitary tumors;(85) as of 2005, no randomized trial comparing resection to percutaneous treatments; recurrence rates similar to those for post resection(21). However a comparative study found that local therapy can achieve a 5-year survival rate of around 60% for patients with small HCC.[19,29]

Transcatheter arterial chemoembolization -(TACE)

Transcatheter arterial chemoembolization (TACE) is usually performed for unresectable tumors or as a temporary treatment while waiting for liver transplant(33). TACE is done by injecting an antineoplastic drug (e.g. cisplatin) mixed with a radioopaque contrast (e.g. Lipiodol) and an embolic agent (e.g. Gelfoam) into the right or left hepatic artery via the groin artery(86,87). By 2005, multiple trials show

objective tumor responses and slowed tumor progression; greatest benefit seen in patients with preserved liver function, absence of vascular invasion, and smallest tumors. TACE is not suitable for big tumors (>8 cm), presence of portal vein thrombus, tumors with portal-systemic shunt and patients with poor liver function.

Radiofrequency ablation

Radiofrequency ablation (RFA) uses high frequency radio-waves to destroy tumor by local heating. The electrodes are inserted into the liver tumor under ultrasound image guidance using percutaneous, laparoscopic or open surgical approach. It is suitable for small tumors (<5 cm). A large randomised trial comparing surgical resection and RFA for small HCC showed similar 4 years-survival and less morbidities.[28]

Radiation therapy

Selective internal radiation therapy can be used to destroy the tumor from within. Currently two products available,(88) SIR-Spheres and Thera Sphere The latter is an FDA approved treatment for primary liver cancer (HCC) which has been shown in clinical trials to increase survival rate of low-risk patients. SIR-Spheres are FDA approved for the treatment of metastatic colorectal cancer but outside the

US SIR-Spheres are approved for the treatment of any non-resectable liver cancer including primary liver cancer.

This method uses a catheter (inserted by a radiologist) to deposit radioactive particles to the area of interest. Intra-arterial iodine-131–lipiodol administration-- Efficacy demonstrated in unresectable patients, those with portal vein thrombus (86). This treatment is also used as adjuvant therapy in resected patients (Lau at et, 1999). It can raise the 3-year survival rate from 46 to 86%. This adjuvant therapy is in phase III clinical trials in Singapore and is available as a standard medical treatment to qualified patients in Hong Kong. Combined PEI and TACE can be used for tumors larger than 4 cm in diameter, but Italian groups have had success with larger tumours using TACE alone.

High intensity focused ultrasound

High intensity focused ultrasound (HIFU) (not to be confused with normal diagnostic ultrasound) is a new technique --- uses much more powerful ultrasound to treat the tumor(90). This technique is still at a very experimental stage.

Hormonal therapy

Antiestrogen therapy with tamoxifen studied in several trials --- mixed results across studies.(32)

Adjuvant chemotherapy

No randomized trials showing benefit of neoadjuvant or adjuvant systemic therapy in HCC.

Palliative treatment

Regimens that included doxorubicin, cisplatin, fluorouracil, interferon, epirubicin, or taxol, as single agents or in combination, have not shown any survival benefit (RR, 0%-25%).

Cryosurgery

Cryosurgery is a new technique that can destroy tumors in a variety of sites (brain, breast, kidney, prostate, liver). Cryosurgery is the destruction of abnormal tissue using sub-zero temperatures(90). Cryosurgery involves the placement of a stainless steel probe into the center of the tumor. Liquid nitrogen is circulated through the end of this device.

The tumor and a half inch margin of normal liver are frozen to -190°C for 15 minutes, which is lethal to all tissues. The area is thawed for 10 minutes and then re-frozen to -190°C for another 15 minutes. After the tumor has thawed, the probe is removed, bleeding is controlled, and the procedure is complete. The patient will spend the first post-operative night in the intensive care unit and typically is discharged in 3 – 5 days. Proper selection of patients and attention to detail in performing the cryosurgical procedure are mandatory in order to achieve good results and outcomes.

Frequently, cryosurgery is used in conjunction with liver resection as some of the tumors are removed while others are treated with cryosurgery.

MATERIALS & METHODS

This descriptive study was carried out in the Department of Medical Gastroenterology and Hepatology, Stanley Medical College, Chennai. This is the major referral tertiary care center available to the population of Tamilnadu, Pondicherry and neighboring states Andhra Pradesh and Karnataka. We have been conducting a prospective surveillance program in patients with cirrhosis with periodical (every 6 months) clinical assessment, AFP levels and US examination of the liver, in order to allow early detection of HCC and to monitor the natural course of the liver disease, onset of complications and long-term outcomes. The college ethical committee approval was obtained.

Using these criteria a total of **201** consecutive patients with cirrhosis, seen in our Department between 2008 and 2011, were included in this study. All patients were followed prospectively with every 6 months ultrasound examination of the liver, clinical and laboratory evaluation, including serum alanine aminotransferase (ALT) and serum AFP levels. Serum HBV and HCV markers (hepatitis B surface antigen (HBsAg) and anti-HCV were also tested at inclusion and during follow-up in all cases, partially by retrospective analysis. Abdominal ultrasound examination was performed with a high resolution real-time instrument

with standardized criteria. Upper abdominal computed tomography (CT) was performed in all patients with focal lesions of the liver detectable and/or with increased levels of AFP (above 200 ng/ml) or peripheral portal thrombosis during follow-up.

Inclusion Criteria

(1) presence of cirrhosis, diagnosed by clinical& lab,imaging findings (presence of shrunken liver, irregular margins and altered liver echo texture at USG, portal hypertension)

(2) Presence of stage A or B disease, according to Child– Turcotte-Pugh, Model for End-Stage Liver Disease classification

(3) Absence of clinical and ultrasonographic evidence of liver cancer at entry with alpha-fetoprotein (AFP) levels <200 ng/ml.

Diagnostic criteria for HCC

1. **Radiological criteria:** two coincident imaging techniques with Focal lesion >2 cm with arterial hypervascularization.

2. **Combined criteria:** one imaging technique associated with AFP Focal lesion >2 cm with arterial hypervascularization.

AFP levels >200 ng/ml diagnosis of Hepatocellular carcinoma.

Exclusion Criteria

Patients who have been diagnosed as

1. Hemangioma of liver

2. Secondaries liver

3. Benign focal liver disorders

Study protocol

At the time of admission a detailed history was obtained from the patients or care given. Their details entered in a preformed proforma (Annexure). They were enquired about presenting complaints, the duration of illness, past h/o jaundice, blood transfusion. Detailed history of alcoholism and status of chronic liver disease and their treatment details obtained. Patients were carefully examined at the time of admission. Various clinical parameters studied which include jaundice, pallor, stigmata of chronic liver disease. Enlarged liver was looked for along with size, surface, border and bruit. Splenomegaly, free fluid and neurological status were assessed. Stage of the liver disease assessed

based on Child-Turcotte-Pugh (CTP), Model for End-Stage Liver Disease (MELD) Classification

Table 1. The Child–Pugh Classification System

Variable	Score 1	Score 2	Score 3
Bilirubin (mg/dl)	<2.0	2–3	>3.0
Albumin (g/l)	>3.5	3.5–2.8	<2.8
PT (INR)	<1.7	1.7–2.3	>2.3
Ascites	Absent	Mild to moderate	Severe/refractory
Encephalopathy	Absent	Mild (I–II)	Severe (III–IV)

Model for End-Stage Liver Disease:

MELD uses the patient's values for serum Bilirubin, serum creatinine, and the international normalized ratio for prothrombin time (INR) to predict survival.

It is calculated according to the following formula:

MELD = 3.78[log serum Bilirubin (mg/dL)] + 11.2[Log INR] + 9.57[Log serum creatinine (mg/dL)] + 6.43

The clinical stage and the severity of the disease were assessed based on Barcelona Clinic Liver Cancer stage.

Table 2: The Barcelona Clinic Liver Cancer Staging Classification of patients with Hepatocellular carcinoma (5)

Staging	**Performance status**	**Tumor stage**	**Child-Pugh**
(A)Early	0	Single <5 cm, 3 nodes <3 cm	A & B
(B) Intermediate	0	Large/multinodular	A & B
(C) Advanced	1-2	Vascular invasion extra hepatic spread	A & B
(D) End-stage	3-4	Any of the above	C

All the patients enrolled in the study were investigated as outlined in the Proforma (Annexure). Patients were subjected for radiological investigations including ultrasound abdomen, Contrast enhanced Computed tomography (CECT) abdomen or MRI, whichever is feasible. Blood samples were collected for viral markers such as HBsAg, anti-HCV antibody, HIV serology, Liver function tests, and serum alpha

fetoprotein (AFP). Ascitic fluid collected for biochemical investigations. Upper GI endoscopy was done to assess the grade of varices and any evidence of portal hypertension. After admission, once clinical diagnosis was made appropriate therapy was instituted.

Serologic testing

Anti-HCV was determined by second generation enzyme-linked immunosorbent assay and by second generation recombinant immunoblotting assay. Hepatitis B surface antigen was detected by commercially available kits.

Statistical methods

The SPSS 16.0 version software was used for statistical analysis. The quantitative data were presented as mean±SD or median (range). The Kruskal–Wallis test was used to compare a continuous variable across different stages of tumors. The P-value<0.05 for univariate analysis and less than 0.1 for multivariate analysis was considered statistically significant. Univariate analysis by the Student's t-test was used to compare age and duration and stage of cirrhosis at tumor diagnosis, as well as ALT and AFP behavior during follow-up and etiological factors of liver disease in relation to the pattern of HCC.

RESULTS

Baseline characteristics

Two-hundred one (201) patients who fulfilled the study criteria were included in the present study. Table 1 reveals that the mean age was 55 years with male female ratio of 5:1 (Figure 1). Out of 201 patients **only 49 (24%)** patients developed HCC, in a mean period of 30.2±6 months and range of 22 –40 months. Socio-economic status was described in Table 2.

Age distribution

The age distribution among the study population is summarized in Fig 2. Nearly half of the patients belong to the age group of 55 to 65 years. Mean age for male was 56.4± 10.6 and 48.4 ± 11 for female. Overall mean age was 55.1± 11. Nearly less than 10 percent of patients either belong to 40-50 years or more than 70 years of age.

Clinical features at presentation

Among the symptoms abdominal pain and weight loss was **most commonly** observed symptoms. (Table 3, Figure 3) More than half of the patients had anorexia and or weight loss. The features of **hepatic decompensation were seen in half** the patients at first presentation with

Ascites in 52.8%, jaundice in 15.9% and hepatic encephalopathy in 3.8% of patients. Gastrointestinal bleed / melena present only in 1.4% patients. Hepatomegaly was seen in more than half the patients (67.8%) while in 26% of cases liver was not enlarged (Table 4, figure4). The enlarged liver was hard in two-third cases and was firm in consistency in the remaining one third. Clubbing, hepatic bruit and were less common. 11(22.4%) patients had a Child–Pugh stage C and 18 (36.7%) stage B and stage A 20(40.8%) cirrhosis. MELD score was 6-24 range and mean was 11.

Table 1 Baseline characteristics of patients with HCC

Parameters	N=49
Age (years) **Median (range)** **Mean± SD**	 **55(29-85)** **55.1±11**
Sex (M : F)	**41:8**
Symptom duration before HCC diagnosis(months) **Median (range)** **<6 month (%)** **>6 month (%)**	 **5.6(4-10)** **44.9** **45.1**

Figure. 1

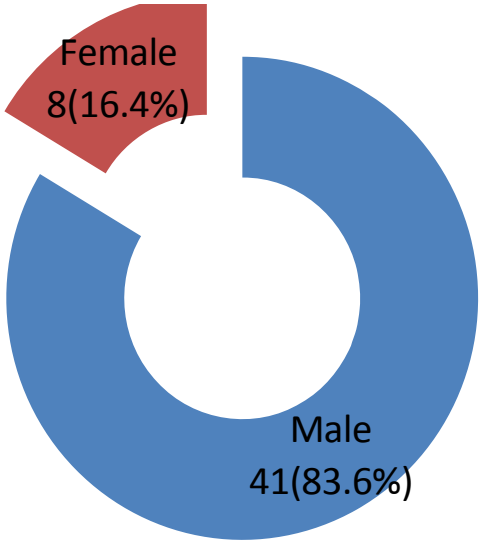


Table 2: Socio-economic status

Income Group (Rs/month)	No. of cases	Percentage
<4000	29	59.2%
4000-8000	14	28.56%
>8000	6	12.2%

Table 3: Symptomolgy of HCC

Symptoms	No. of patients	Percentage (%)
Abdominal Pain	39	79.6
Loss of weight/ appetite	17	34.7
Ascites	16	32.7
UGI bleeding	8	16.3
Edema of legs	7	14.3
Jaundice	6	12.2
Oliguria	2	4.1
Fever	2	4.1

Figure. 2

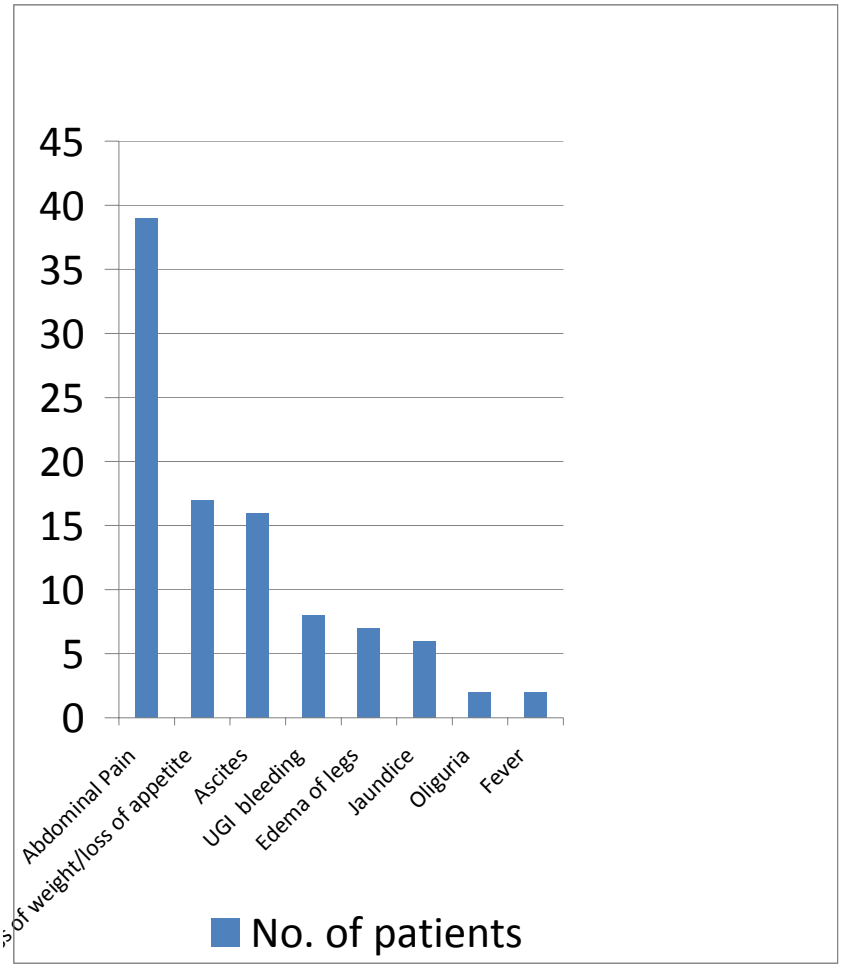
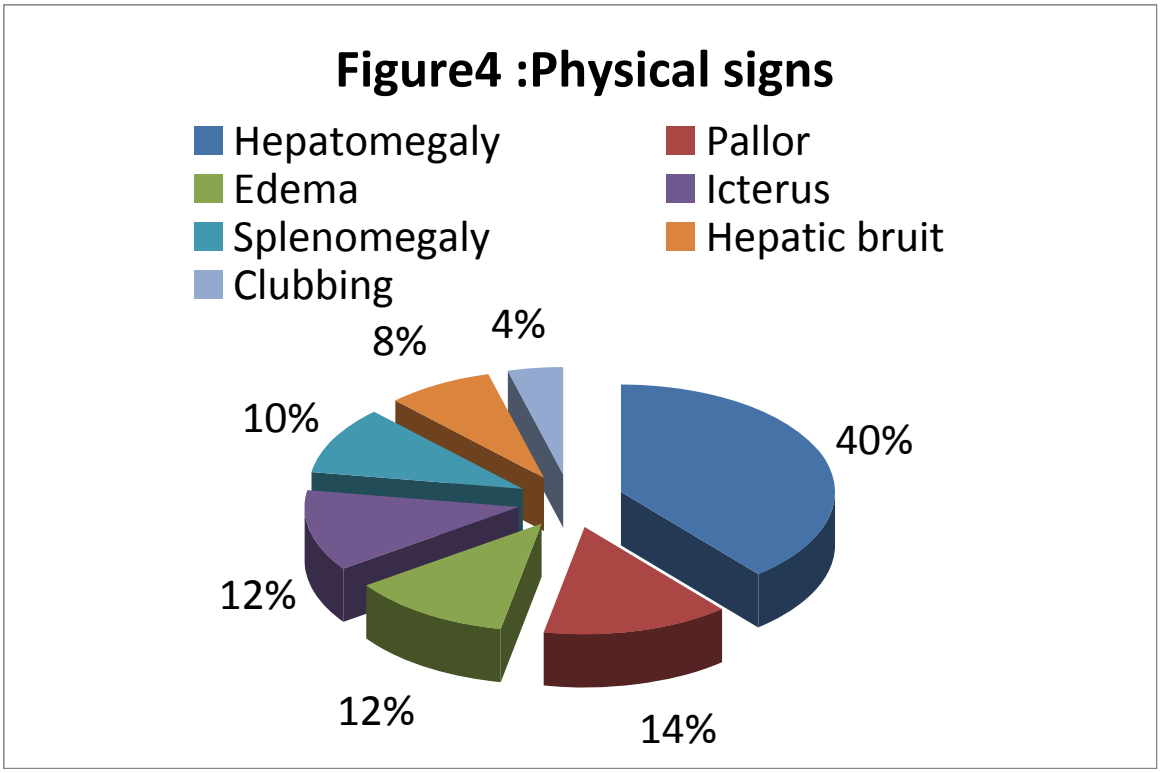

45
40
35
30
25
20
15
10
5
0
Abdominal Pain
s of weight/loss of appetite
Ascites
UGI bleeding
Edema of legs
Jaundice
Oliguria
Fever
No. of patients

Table 4: Physical signs of HCC

Physical signs	No. of patients	Percentage (%)
Hepatomegaly	19	38.7
Pallor	7	14.2
Edema	6	12.2
Icterus	6	12.2
Splenomegaly	5	10.2
Hepatic bruit	4	8.6
Clubbing	2	4



Hematological, biochemical and endoscopic profile

The biochemical investigations were mildly deranged. Serum alpha fetoprotein (AFP) was diagnostic (>200 ng/ml) in **27 of 49 (55.1%)** patients; with normal AFP in 9 (18.3%) patients. The median serum AFP value was **786 ng/ml** (range 0.04–98422). Mean AST and ALT values were more than two time of upper limit of normal. The mean serum Bilirubin was 5.4±2. More than three fourth of cases had esophageal varices with gastric varices of 19.1%. Nearly three fourth of cases had low serum albumin level of <2.8 gm.

Incidence and risk factors of HCC in HBV and in HCV associated cirrhosis

Seventeen (34.7%) were positive for HBsAg and 18 (36.7%) were positive for anti-HCV patients developed HCC .

Table 4: Etiology of HCC.

Etiology	**No. (%)**
Cryptogenic	**4(8.1)**
HBV related	**17(34.7)**
HCV related	**18 (36.7%)**
Alcohol alone	**9(18.4)**
HBV+HCV	**1(2)**
Alcohol +HCV	**5(10.2)**
Alcohol +HBV	**3(6.1)**
Alcohol +HBV+HCV	**1(2)**

Radiological studies

Two different macroscopic patterns of HCC development were observed on the basis of US or CT findings (tumor margin, presence or absence of peri-nodular capsule : (1) tumor arising as a small, capsulated nodule, with well-defined margins and expansive growth (nodular type) and, (2) tumor presenting as a spreading mass not clearly defined, with ill-defined margins and infiltrative growth (infiltrating type).

Very large tumors (>5 cm) were seen in 2/3 (two-third) of cases.

The average size of HCC was 6±4 cm. Small HCC (<2 cm lesion) was seen in only 6% of patients approximately (Table 6). Single lesion was the most common presentation of HCC observed in two-third cases. Three or more lesions were seen in about one-fifth of cases. During follow-up, HCC developed as nodular type in 37 (75.5%) patients, 15(40.5%) with a single nodule and 22(59.5%) with two nodules, while in the remaining 11 (22.4%) cases the tumor developed as an aggressive and infiltrating mass.

On the other hand, male sex HBsAg positivity and dual HBsAg and anti-HCV positivity were significant risk factors for development of infiltrating but not nodular HCC. Vascular invasion of either major

branch of spleno-portal axis was seen in 1/5th of the patients. Main trunk of portal vein or its main branches were involved in **20.8%** patients. The higher risk for infiltrative/diffuse but not for nodular HCC in patients is with HBV infection and with HBV/HCV coinfection.

Table 5: Tumor characteristics of HCC patients

Characteristic	**Patient number (%)**
Tumor size	
<3 cm	**8(15.3)**
3-5cm	**11(20.8)**
>5cm	**30(64)**
Portal vein thrombosis	
No portal vein thrombosis	**37(75.5)**
Main portal vein thrombosis	**12(24.4)**

DISCUSSION

The age distribution of patients with HCC in the present study was similar to other studies in past. Studies from India have shown the maximum incidence of HCC in the fifth to sixth decade.

Our study showed that 43 percent of cases belong to **55 to 65** years of age. Only 10% belongs to 40 – 50 years age group. A very similar observation made by Saini et al (71) HCC commonly observed in male sex. The male preponderance is similar to other studies (68).

The population-based data show a male to female ratio of 3:1–2:1(1). In our study showed male female ration of 5:1. High preponderance of HCC in males in our study could be due to gender bias in seeking medical treatment. And this could be partially explained by the fact that men are more likely to be infected with HBV and HCV, consume alcohol, smoke cigarettes, and have increased iron stores. Hospital based data from various studies made similar observation. (71)

In a series of 461 patients, HBV is the most common etiologic factor in Asian countries. It accounts for up to three-fourth cases of HCC, while HCV infection may account for 10–15% of HCC cases. HBsAg

positivity in our cases was **34.7%,** which is comparable with other Indian studies (36% to 74 %). (68, 71).

The prevalence of anti-HCV antibody in India varies from 0.3% to 1.8%.

In our case series HCV positivity noted only in 36.7% of cases.

Sensitivity of AFP ranges from 39% to 64%, specificity 76–91% and positive predictive value 9–32. 27 of our patients had elevated AFP values beyond diagnostic level. Others had either normal level 7 or levels were in non-diagnostic range. Studies available showing that, serum AFP is frequently elevated in patients with liver cirrhosis without HCC and can be normal or only moderately elevated in patients with Hepatocellular carcinoma.

The median AFP level was only 786 ng/ml in the study population despite advanced HCC was noted in three-fourth cases. There are some studies which suggest that the production of AFP depends on the size or the degree of differentiation of the hepatoma cells.

Clinical parameter comparison - study

Clinical data	SOUTH AFRICA	JAPAN	ITALY	INDIA	My study
Abdominal pain	95	46.2	38	68	**79.6**
Anorexia	25	44.7	6.7	74	**34.7**
Weight loss	34	28.9	8	55	**66.7**
Ascites	51	26.5	17.5	51	**32.7**
Fever	35	16.7	12	36	**4.1**
Jaundice	28	16.7	14	35	**12.2**
Variceal bleed	2	7.6	4	22	**16.3**
Hepatomegaly	-	-	90	84	**81.9**
Palpable mass	92	23.3	-	-	**20.5**
Ankle edema	-	16.8	-	37.5	**12.5**
Asymptomatic	-	-	38	-	**2.8**

Comparison of AFP values – study wise

Study	No, patients	Duration of follow-up	Mean level (ng/ml)
Schwartz et al,2007	102	24.2	618
Paul et l,2007	154	36	>300
Benvengnu et al,2001	401	14	568-645
My study	**201**	**24-30**	**786**

Even when lesions were single, they were large enough in most of the cases to rule out curative resection. Another study from a tertiary care center in India showed that 56% of patients with HCC had tumor size larger than 5cm and high incidence of vascular invasion of main portal vein in 24%.(110) More than half of the patients had a single tumor. Tumor was > 5cm in the majority (64%) of the patients. Moreover portal vein was thrombosed in 24% patient.

Radiological profile of HCC

Characteristic	Kumar et al,2008(%) (110)	Our study(%)	
Distribution of lesion			
RT.LOBE	48	**49.2**	
LT.LOBE	18	**16.4**	
BILOBAR	34	**8.4**	
SIZE OF HCC			
MEDIAN	6.4X6	**6x4**	
>5 CM	73	**64**	
<2CM	7.5	**15.2**	
CT APPEARANCE			
HYPODENSE	42	**45**	
MIXED DENSITY	35	**32**	
HYPERDENSE	23	**9**	

SUMMARY

1. The study includes total of 49 patients, mean age was **55.1 years** with male female ratio of 5:1. Mean age for male was 56.4± 10.6 and 48.4 ± 11 for female

2. Nearly half of the patients belong to the age group of **55 to 65 years**.

3. Mean preadmission duration of illness was **5.6 months**.

4. 2/3 rd belongs to low socio economic status.

5. Among the symptoms abdominal pain (79.6.7%) and weight loss (34.7%) were most commonly observed symptoms.

6. Hepatic decompensation was seen in half the patients at first presentation with Ascites in 52.8%, jaundice in 15.9% and hepatic encephalopathy in 3.8% of patients.

7. The median serum AFP value of **786 ng/ml** (range 0.4–92625) observed in the study population. Diagnostic value of AFP >200 ng/ml was present in 27 of 49 (55.1%) patients; with normal AFP in 9 (18.3%) patient.

8. Hepatomegaly was seen in more than half the patients (67.8%) while in 26% of cases liver was not enlarged

9. 11(22.4%) patients had a Child–Pugh stage C and 18 (36.7%) stage B and stage A 20(40.8%) cirrhosis. MELD score was 6-24 range and mean was 11.

10. **Seventeen** (34.7%) were positive for HBsAg and **18** (36.7%) were positive for anti-HCV patients developed HCC

11. Age above 59 years, male sex, longer duration and more advanced stage of cirrhosis were significant risk factors for HCC in anti-HCV positive cirrhotic patients, while none of these variables were significant risk factors for HCC in HBsAg positive patients.

12. HBsAg positive patients -- presence of high or fluctuating serum AFP levels during follow-up was a significant risk factor for tumor development.

13. Mean AST and ALT values were more than two time of upper limit of normal. The mean serum Bilirubin was 5.4±2.

14. More than 3/4th of cases had esophageal varices with gastric varices of 19.1%.

15. Nearly 3/4th of cases had low serum albumin level of <2.8 gm.

16. Very large tumors (>5 cm) were seen in two-third of cases. The average size of HCC was 6±4 cm. Small HCC (<2 cm lesion) was seen in only 6% of patients approximately.

17. HCC developed as nodular type in 37 (75.5%) patients, 15(40.5%) with a single nodule and 22(59.5%) with two nodules, while in the remaining 11 (22.4%) cases the tumor developed as an aggressive and infiltrating mass.

18. Male sex, HBsAg positivity and dual HBsAg and anti-HCV positivity were significant risk factors for development of infiltrating but not nodular HCC.

19. The higher risk for infiltrative/diffuse but not for nodular HCC is seen in patients with HBV infection and with HBV/HCV coinfection.

CONCLUSION

1) In our study --- **Age above 59 years, male sex, longer duration and more advanced stage of cirrhosis were significant risk factors** for HCC in anti-HCV positive cirrhotic patients, while none of these variables were significant risk factors for HCC in HBsAg positive patients.

2) In our study --- **high AFP** fetoprotein predicts early development of HCC in cirrhotics.

3) In our study --- higher risk for infiltrative / diffuse but not for nodular HCC is seen in patients wit**h HBV infection and with HBV/HCV coinfection**.

4) In our study -- mean duration of survival after the diagnosis is <9 months.

5) In our study -- The paraneoplastic manifestations are distinctly rare.

6) In our study -- HCC is diagnosed very late and presents with vascular invasion or metastases in most of the cases

7) In our study --Since HBV is one of most common etiologic agent, the universal vaccination against hepatitis B would prove an effective preventive strategy.

MASTER CHART

Diagnosis	Name	Age	Sex	DOR	MGENo	Per capita income Rs/month	Ascites	Duration of ascites	Jaundice	Abdominal pain	LOW LOA	Duration	HBV	Alcohol History	Duration	Amount ml day	Pallor	Icterus	Pedal edema	Palpable	Surface	Border	Consistenc	HBsAG	Anti HCV	Hb	TC	DC	Platelet	PCV	PT	INR	Sugar	Urea	Creatinine	TB/DB	AST	ALT	AG	SAP	AFP above 200	AFP	MELD	CTP	Survival after diagnosis	CT Size of tumour
HCV related DCLD/PHT/HCC right lobe (child A)	Mr Anbalagan	52	0	22-Sep-08	1386/08	3000	FALSE		FALSE	TRUE	FALSE	1 year	FALSE	1	10	80	FALSE	FALSE	FALSE	FALSE				FALSE	TRUE	12.8	5700	P58L32E10	280000	39.7	15/14	1.1	279	20.6	1.0	1.02/0.97	95	66	4.1/4.1	160	0	20.1	11	A	18	7.5x6.5
Cirrhosis of liver/ascites/advanced HCC right lobe	Mr Chinnaswami	72	0	24-Dec-08	5162/08	4000	TRUE	20 days	FALSE	TRUE	FALSE	1 month	FALSE	2	10	180	FALSE	FALSE	TRUE	FALSE				FALSE	FALSE	11.6	11800	P81L12E07	108000	36.5	13/17	1.4	61	39	1.13	33.9/23.6	421	252	3.5/3.4	380	0	18.4	24	B	7	
HBV related DCLD/PHT/Advanced HCC/palliation Chemotherapy	Mr Chinnaswami	50	0	14-Nov-08	47191/08	5000	FALSE		FALSE	TRUE	FALSE	1 year	FALSE	0			FALSE	FALSE	TRUE	TRUE	1	0		TRUE	FALSE	9.3	7600	P52L30E09	234000	32	15/15	1.0	176	33	0.9	1.20/0.77	92	42	3.4/3.8	121	-1	450	6	A	5	1.4x1
DCLD/PHD/ethanol related/HCC right lobe/post RFA	Mr Krishnamurthi	85	0	25-Nov-08	48482/08	5000	TRUE	6 months	FALSE	FALSE	FALSE		FALSE	0			TRUE	TRUE	TRUE	TRUE	1	0	0	FALSE	FALSE	9.5	4100	P69L29E10	103000	29.4	15/15	1.0	118	25.7	0.8	2.7/1.53	100	79	3.5/4.7	422	-1	598	8	A	9	3x3
HBV related DCLD/PHT/HCC 6&7 child B/resection of segment 6&7	Mr Powee	55	0	18-Aug-08	36428/08	25000	FALSE		FALSE	TRUE	TRUE	3 months	FALSE	0			FALSE	TRUE	FALSE	TRUE	1	0		TRUE	FALSE	12	11000	P77L13E10	210000	37	15/16	1.1	77	14	1.1	3.3/2.4	84	32	2.9/4.5	244	0	64.89	13	B		8x6.5
HCV related DCLD/PHT/Advanced HCC/PVT/transient chemotherapy	Mr Nataranjan	58	0	08-Nov-10	39732/10	8000	FALSE		FALSE	FALSE	FALSE		FALSE	0			FALSE	FALSE	FALSE	FALSE				FALSE	TRUE	13.8	6800	P67L28E05	179000	43.8	15/14	1	153	26.2	0.78	1.26/0.8	56	51	4.0/2.7	240	-1	206.7	6	A	8	
HCV related DCLD/PHT/HCC right lobe	Mr Dakshinamurthy	61	0	25-Mar-09	10108/09	3000	FALSE		FALSE	FALSE	FALSE		FALSE	0			FALSE	FALSE	FALSE	FALSE				FALSE	TRUE	12.7	9300	P60L30E10	127000	39.4	15/17	1.2	71	24	1.3	0.41/0.29	124	68	3.3/4.3	290	0	3.24	11	A	9	6.1x5.6
HCV related DCLD/PHT/Advanced HCC right lobe	Mr Bhaskar	62	0	23-Feb-09	6442/09	3000	FALSE		FALSE	TRUE	FALSE	2 months	FALSE	1	15	180	FALSE	FALSE	TRUE	TRUE	1	0	0	FALSE	TRUE	12.8	9100	P69L23E08	196000	41.2	15/14	1.0	95	25	0.7	0.8/0.41	665	119	3.2/3.7	670	0	161	6	A	8	8x6
HCV related DCLD/PHT/HCC/PVT	Mr Mathivanan	42	0	23-Mar-09	11862/09	4000	TRUE	3 months	FALSE	TRUE	FALSE	2 months	FALSE	0			TRUE	TRUE	TRUE	TRUE	1	0	1	FALSE	TRUE	10.2	10500	P74L16E10	290000	32	15/18	1.3	120	11.7	0.7	3.4/2.6	282	227	2.1/5.8	386	-1	4553	11	B	4	
HBV related DCLD/PHT/HCC with PVT left lobe	Mr Murlikrishnan	57	0	09-May-09	15379/09	4000	FALSE		FALSE	TRUE	FALSE	2 months	FALSE	0			TRUE	FALSE	FALSE	TRUE	0	0	0	TRUE	FALSE	11.7	13300	P70L28E02	335000	36.6	15/15	1.0	100	29	1.4	0.4/0.3	26	07	3/4.8	377	-1	1086	10	A	12	
HCV related DCLD/PHT/bilobar HCC with PVT	Mr Parchigam	49	0	30-Jan-09	3346/09	3000	TRUE	1 month	TRUE	TRUE	FALSE	1 month	FALSE	0			FALSE	TRUE	TRUE	TRUE	1	0	1	FALSE	TRUE	13.1	5900	P60L30E10	161000	42.2	15/14	1.0	114	15.7	1.2	3.1/2.2	100	93	3.4/3.6	46	-1	786	12	B	5	
HCV related DCLD/PHT/HCC RFA done	Mrs Pappamal	48	1	18-Feb-09	5743/11	2000	FALSE		FALSE	TRUE	TRUE	3 months	FALSE	0			TRUE	FALSE	FALSE	TRUE	0	0	1	FALSE	FALSE	9.6	10000	P50L40E10	23000	28.8	15/21	1.5	196	19.7	0.5	1.0/0.81	109	69	3/3.5	502	-1	650.56	6	A	14	4x3.8
Ethanol related DCLD/PHT/HCC/PVT(main PV)	Mr Deengaswamy	60	0	24-Dec-08	51650/08	5000	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	2	15	180	FALSE	TRUE	TRUE	TRUE	0	0	1	FALSE	FALSE	12.1	11300	P83L03E08	358000	38	15/21	1.5	127	19.9	0.5	1.6/1.1	85	87	3.3/3.7	761	0	35.8	6	A	6	
HBV related DCLD/PHT/advanced HCC	Mr Gopal	58	0	06-Feb-09	4279/09	3000	FALSE		FALSE	TRUE	FALSE	2 months	FALSE	0			FALSE	FALSE	TRUE	TRUE	0	0		FALSE	FALSE	13	7300	P50L40E10	250000	31	15/14	1.0	70	31	0.5	1.0/0.4	122	134	3.6/4.4	305	-1	1134	6	A	13	6x7
HBV related DCLD/PHT/HCC left lobe	Mr Govindan	56	0	12-Feb-09	1897/09	4000	FALSE		FALSE	TRUE	TRUE	3 months	FALSE	2	10	180	TRUE	FALSE	TRUE	TRUE	1	0	1	TRUE	FALSE	10.8	7000	P60L35E05	347000	34	15/17	1.2	87	31	0.6	1.6/0.54	86	57	2.9/3.2	868	-1	587	6	A	5	12.4x12
Ethanol related DCLD/PHT/advanced HCC	Mr Sampath Kumar	52	0	17-Feb-09	5614/09	3500	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	1	10	270	TRUE	TRUE	TRUE	TRUE	1	0		FALSE	FALSE	8.6	11600	P81L42E07	565000	25	14/15	1.0	150	28	1.0	2.9/1.4	308	95	2.8/4.7	1309	-1	60500	10	B	5	
Ethanol related DCLD/PHT/HCC advanced right lobe of liver	Mr Syed Ebrahim	67	0	23-Dec-08	51563/08	6000	TRUE	4 months	TRUE	TRUE	FALSE	1 month	FALSE	1	15	180	FALSE	TRUE	TRUE	TRUE	1	0	1	FALSE	FALSE	12.7	9100	P72L18E10	344000	40	15/15	1.0	326	28	0.6	7.3/5.0	98	56	3.2/3.4	816	-1	3000	9	B	5	
HCV related DCLD/PHT/Cheld A/HCC right lobe	Mr Anbagham	52	0	22-Sep-08	40558/08	3000	FALSE		FALSE	TRUE	FALSE	1 year	FALSE	2	10	180	FALSE	FALSE	FALSE	TRUE	0	0	1	FALSE	TRUE	12.8	5700	P58L32E10	280000	39.7	15/14	1.0	279	20.6	1.0	1.02/0.97	95	66	4.1/4.1	160	0	20.1	6	A		7.5x6.5
HCV related DCLD/PHT/HCC right lobe	Mr Dhanasekharan	51	0	21-Nov-09	39743/09	10000	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	0			TRUE	FALSE	TRUE	TRUE	1	0		FALSE	TRUE	7.1	1300	P45L45E10	47000	22	15/22	1.8	157	19	1.2	1.7/1.4	57	22	2.3/2.5	205	0	43.1	17	B	5	
HCV related DCLD/PHT/HCC right lobe liver	Mr Manikkam	59	0	04-May-10	15523/10	4500	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	0			TRUE	FALSE	FALSE	FALSE				FALSE	TRUE	10.8	7200	P60L30E10	457000	37.5	15/14	1.0	183	17.7	0.8	1.0/0.95	26	14	4.1/3.7	185	-1	215.71	6	A	11	1.3x1
HCV related DCLD/PHT/Multicentric HCC/old MI	Mr Arulsamy	69	0	20-Mar-10	9992/10	5000	FALSE		FALSE	TRUE	FALSE	15 days	FALSE	0			FALSE	FALSE	FALSE	TRUE	1	0		FALSE	TRUE	12.7	9300	P60L30E10	198000	39.4	15/14	1.0	127	25.5	0.65	0.9/0.6	124	51	3.7/3.2	254	-1	3000	6	A	5	10x8
HCV related DCLD/PHT/HCC left lobe	Mr Arumugam	60	0	09-Dec-10	43398/10	2000	FALSE		FALSE	TRUE	FALSE	3 months	FALSE	2	10	180	TRUE	FALSE	FALSE	TRUE	0	0		FALSE	TRUE	11.4	6900	P65L26E09	126000	35.7	15/14	1.0	112	35.4	1.06	1.2/0.69	105	78	3.6/4.9	501	0	1	8	A	9	3x1
HBV/DCLD/PHT/HCC right lobe	Mrs Parimala	60	1	28-Feb-11	7426/11		TRUE	2 months	FALSE	FALSE	FALSE		FALSE	0			TRUE	FALSE	TRUE	TRUE	1	0	1	TRUE	FALSE	9.7	6900	P76L17E07	223000	29.9	14/19	1.4	123	17.0	0.9	0.74/0.55	66	40	2.3/7.9	210	-1	686	8	A	6	9.2x9
DCLD/PHT/multifocal HCC/BCS	Mrs Chinnapappa	35	1	07-Dec-10	20313/10	2000	FALSE		FALSE	TRUE	FALSE	6 months	FALSE	0			TRUE	FALSE	TRUE	TRUE	0	0	0	FALSE	FALSE	7.5	6900	P65L26E09	113000	39.2	15/14	1.0	119	23.4	0.82	0.71/0.34	57	32	3.8/4.3	327	-1	>1000	6	A	9	6.7x5
HCV related DCLD/PHT/HCC right lobe	Mr Krishnamoorthy	76	0	26-Nov-10	42013/10	2000	TRUE	1 month	FALSE	TRUE	FALSE	2 months	FALSE	0			TRUE	FALSE	TRUE	TRUE	1	1	1	FALSE	TRUE	8.9	13500	P72L20E08	91000	46.1	15/14	1.0	117	47.4	1.12	1.3/0.9	25	29	2.4/3.6	137	-1	768	9	A	8	8x6.4
HBV related DCLD/PHT/Multicentric HCC/SHT/CAHD	Mrs Malliya	56	1	21-Jan-10	2517/10	1500	FALSE		TRUE	FALSE	TRUE		FALSE	0			TRUE	TRUE	FALSE	TRUE	1	0	1	TRUE	FALSE	10.8	2900	P75L16E09	44000	34.1	15/16	1.0	99	32	1.0	1.2/1.0	27	97	2.5/3.3	332	0	12.8	7	A	9	
HCV related DCLD/PHT/Multicentric HCC	Mr Maran	55	0	19-Jul-10	25269/10	3000	FALSE		FALSE	TRUE	FALSE	2 months	FALSE	2	10	180	FALSE	FALSE	FALSE	TRUE	1	1	1	FALSE	TRUE	15.6	13500	P72L20E08	166000	46.1	15/14	1.0	160	31.3	0.77	1.0/0.6	25	29	4.4/2.7	206	-1	592	6	A	7	
Ethanol related DCLD/PHT/HCC	Mr Venkateshaw	45	0	09-Jan-10	1106/10	3000	FALSE		FALSE	TRUE	FALSE	6 months	FALSE	2	15	90	TRUE	FALSE	FALSE	TRUE	0	0	1	FALSE	FALSE	10.9	5900	P72L20E08	106000	32	14/15	1.0	268	19	0.44	1.2/0.8	79	57	2.6/4.7	402	-1	851	6	A	13	7.3x6.1
Ethanol related DCLD/PHT/HCC	Mr Kalyana Sundaram	71	0	30-Dec-10	45656/10	3000	TRUE	6 months	FALSE	FALSE	FALSE		FALSE	2	10	180	TRUE	FALSE	TRUE	FALSE				FALSE	FALSE	4.7	3600	P66L19E10	138000	16.9	14/16	1.2	150	26.3	0.85	7.2/5.6	57	25	3.4/2.8	229	0	4	14	B	9	5.8x5.7
HBV related DCLD/PHT/Advanced HCC/PVTright lobe	Mrs Nasima	30	1	03-Jan-11	271/11		FALSE		FALSE	TRUE	FALSE	1 month	FALSE	0			TRUE	FALSE	TRUE	TRUE	1	0	1	TRUE	FALSE	7.3	4400	P66L20E10	148000	27.3	15/14	1.0	116	19.2	0.47	1.28/0.8	107	32	3.4/4.2	338	-1	300000	6	A	5	13.7x12.8
HBV related DCLD/PHT/Advanced HCC	Mr Ibrahim	47	0	15-Jul-11	24817/10	3000	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	2	10	180	FALSE	FALSE	FALSE	TRUE	0	0	1	TRUE	FALSE	13.3	8500	P71L21E08	394000	44.9	15/14	1.0	112	16.5	0.84	1.0/0.6	111	47	3.6/3.7	218	-1	605000	6	A	8	9.4x6.5
HBV related DCLD/PHT/HCC right lobe	Mr Pedhutu	29	0	13-Aug-09	27327/09	4000	FALSE		FALSE	TRUE	TRUE	2 months	FALSE	0			FALSE	FALSE	FALSE	FALSE				TRUE	FALSE	16	8600	P65L31E04	305000	50.9	15/14	1.0	64	22	0.8	1.2/0.9	20	66	3.4/3,1	2073	0	70.7	6	A	6	20x20
HBV related DCLD/PHT/Bilobar Multicentric HCC	Mrs Tamilarasi	50	1	12-Nov-10	40242/10		FALSE		FALSE	TRUE	TRUE	4 months	FALSE	0			TRUE	FALSE	FALSE	TRUE	1	0	1	TRUE	FALSE	12.3	10400	P75L20E10	352000	42.7	15/15	1.0	73	20	0.8	1.4/0.87	135	135	3.3/3.1	1812	0	12.2	6	A	6	
HCV related DCLD/PHT/HCC	Mr Raman	70	0	16-Nov-10	40785/10		FALSE		FALSE	TRUE	FALSE	6 months	FALSE	2	15	180	TRUE	FALSE	FALSE	TRUE	1	0	1	FALSE	TRUE	11	8200	P69L25E06	392000	34	14/14	1.0	492	30.1	0.9	0.79/0.33	109	33	3.6/3.2	2961	0	0.2	6	A	12	13.5x11.7
HBV related DCLD/PHT/Advanced HCC	Mr Chella Durai	47	0	15-Apr-11	12869/11	3000	TRUE	6 months	FALSE	TRUE	TRUE	1 year	FALSE	0			TRUE	TRUE	TRUE	TRUE	0	0	1	TRUE	FALSE	11.1	6200	P64L24E10	114000	36.5	15/14	1.0	92	19.1	0.7	2.1/1.0	200	183	3.5/3.9	1526	-1	986	6	A	3	
Ethanol related DCLD/PHT/multicentric HCC/child B	Mr Kalliyannan	61	0	03-Jan-11	221/11	3000	FALSE		FALSE	TRUE	TRUE	3 years	FALSE	0			FALSE	FALSE	FALSE	TRUE	1	0	1	FALSE	FALSE	7.5	5300	P71L21E08	85000	27.3	15/15	1.1	95	21	0.6	0.9/0.55	39	27	2.8/3.9	267	0	1.35	6	A	4	5x4
Ethanol related DCLD/PHT/HCC	Mr Pardaram	48	0	07-Nov-09	38016/09	3000	TRUE	1 month	FALSE	TRUE	TRUE	1 month	FALSE	1	10	180	TRUE	TRUE	TRUE	TRUE	1	0	1	FALSE	FALSE	11.2	8600	P80L10E10	133000	36.6	15/17	1.3	80	30.2	0.8	6.1/4.0	128	48	1.9/3.2	1128	0	5.28	14	B	4	
HBV related DCLD/PHT/HCC/locally advanced	Mr Sekhar	44	0	31-Dec-09	44779/09	5000	FALSE		FALSE	TRUE	TRUE	3 months	FALSE	1	10	180	TRUE	FALSE	FALSE	TRUE	1	0	0	TRUE	FALSE	11.9	11900	P74L16E10	430000	40.4	15/16	1.1	125	17.8	0.8	1.5/1.1	54	30	3.5/2.6	928	-1	>3000	7	A	10	11.5x7.2
HBV related DCLD/PHT/HCC right lobe	Mrs Vellachi	48	1	13-Jul-10	24520/10		FALSE		FALSE	TRUE	FALSE	1 month	FALSE	0			TRUE	FALSE	FALSE	TRUE	0	0	0	TRUE	FALSE	11.3	7000	P65L25E10	309000	37.9	15/14	1.0	139	22.3	0.75	0.9/0.5	100	56	2.8/2.5	214	-1	>3000	6	A		10.5x9.5
HCV related DCLD/PHT/HCC right lobe	Mr Mannikam	59	0	19-May-10	2470/10	11000	FALSE		TRUE	TRUE	TRUE	1 month	FALSE	2		occasional	FALSE	TRUE	FALSE	FALSE				FALSE	TRUE	10.8	7200	P60L30E10	457000	32.2	14/26	1.2	183	17.7	0.8	1.0/0.95	26	14	4.1/3.7	185	-1	215.71	6	A	4	

Ethanol related DCLD/PHT/HE/type 2 DM/HCC	Mr Padmanabham	72	0	23-Apr-11	2169/11	5000	TRUE	6 months	FALSE	FALSE	FALSE		FALSE	2	7		TRUE	FALSE	FALSE	FALSE				TRUE	FALSE	12.9	8200	P80L09E11	90000	40.9	14/16	1.1	106	33.94	0.76	1.2/0.8	109	31	2.3/2.4	263	-1	705	6	A		8.5x8.1
HCV related DCLD/PHT/SBP/HCC/PVT	Mr Jhukkanam	48	0	28-Jan-11	225/11	2500	TRUE	3 months	TRUE	TRUE	FALSE	2 months	FALSE	2	13	180	TRUE	TRUE	FALSE	TRUE		0	0	FALSE	TRUE	14	11100	P70L20E10	146000	42.7	14/15	1.0	194	41.2	0.56	3.4/1.9	216	63	3.5/3.4	555	-1	11435	6	A		
HCV related DCLD/PHT/DM/HCC	Mr Ramagle	47	0	11-Jan-11	499/11	12000	FALSE		FALSE	TRUE	FALSE	3 months	FALSE	0			FALSE	FALSE	FALSE	TRUE	1	0	0	FALSE	TRUE	13.9	10100	P65L25E10	281000	43.1	14/22	1.9	95	11.7	0.6	0.8/0.5	36	39	2.9/3.6	431	-1	435.6	7	A	4	
HBV related DCLD/PHT/PVT/PCC	Mr Mohandas	55	0	26-Jan-11	246/11		FALSE		FALSE	FALSE	TRUE		FALSE	0			FALSE	FALSE	FALSE	TRUE	1		1	TRUE	FALSE	10.7	11400	P81L10E09	145000	35.3	15/18	1.3	155	23.82	0.64	1.59/0.99	71	25	2.7/4.7	500		256	6	A		6.9x7.1
HBV related DCLD/PHT/HCC/non alcoholic	Mrs Parimala	60	1	12-Jan-11	319/11		TRUE	1 month	FALSE	FALSE	TRUE		FALSE	0			TRUE	FALSE	FALSE	TRUE	1	0	1	TRUE	FALSE	9.2	6900	P67L20E13	255000	29.1	15/17	26/28	286	10.33	0.63	1.25/0.66	69	37	2.1/4.7	209		12.3	7	B	6	9.2x9
HBsAg DCLD/PHT/HCC	Mr Ragu	60	0		7053/10		TRUE	3 months	TRUE	TRUE	TRUE	2 months	FALSE	0			TRUE	TRUE	FALSE	TRUE	1	0	0	FALSE	FALSE	10.2	7600	P80L20	120000	33	15/18	1.3	176	30.4	0.9	1.0/0.8	56	48	2/3.2	308		392	14	A	7	
HBV related DCLD/PHT/HCC	Mr Mahadevan	56	0		149/09		TRUE	3 months	FALSE	FALSE	TRUE		FALSE	0			FALSE	FALSE	FALSE	TRUE	0	0	0	TRUE	FALSE	9.2	3800	P74L18	85000	32	19	1.3	74	14	0.7	1.4/0.8	63	32	2.1/4.7	190		0.4	6	A	7	8.1x8
HBV related DCLD/PHT/HCC	Mr Sundaraj	42	0		3012/10		FALSE		FALSE	TRUE	TRUE	6 months	FALSE	2	8	180	TRUE	FALSE	FALSE	TRUE	0	0	0	TRUE	FALSE	16.3	7000	P60L30E10	171000	51.3	16	1.2	85	23.3	0.91	1.4/1.0	410	83	3.3/3.8	467		3000	6	B	7	
HCV related DCLD/PHT/PVT/multicentric HCC	Mr Balasubhramaniam	56	0	09-Mar-10	1254/10		TRUE	2 months	FALSE	TRUE	TRUE	1 week	FALSE	0			FALSE	FALSE	FALSE	TRUE	1	0	0	FALSE	TRUE	13.1	6400	P80L13E07	14000	41.1	18	1.3	95	41.1	0.68	5.2/3.7	17	126	2.5/3.9	697		721.67	6	A	9	4.1x3.4

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MASTER CHART

Diagnosis	Name	Age	Sex	DOR	MGENo	Per capita income Rs/month	Ascites	Duration of ascites	Jaundice	Abdominal pain	LOW LOA	Duration	HBV	Alcohol History	Duration	Amount ml day	Pallor	Icterus	Pedal edema	Palpable	Surface	Border	Consistenc	HBsAG	Anti HCV	Hb	TC	DC	Platelet	PCV	PT	INR	Sugar	Urea	Creatinine	TB/DB	AST	ALT	AG	SAP	AFP above 200	AFP	MELD	CTP	Survival after diagnosis	CT Size of tumour
HCV related DCLD/PHT/HCC right lobe (child A)	Mr Anbalagan	52	0	22-Sep-08	1386/08	3000	FALSE		FALSE	TRUE	FALSE	1 year	FALSE	1	10	80	FALSE	FALSE	FALSE	FALSE				FALSE	TRUE	12.8	5700	P58L32E10	280000	39.7	15/14	1.1	279	20.6	1.0	1.02/0.97	95	66	4.1/4.1	160	0	20.1	11	A	18	7.5x6.5
Cirrhosis of liver/ascites/advanced HCC right lobe	Mr Chinnaswami	72	0	24-Dec-08	5162/08	4000	TRUE	20 days	FALSE	TRUE	FALSE	1 month	FALSE	2	10	180	FALSE	FALSE	TRUE	FALSE				FALSE	FALSE	11.6	11800	P81L12E07	108000	36.5	13/17	1.4	61	39	1.13	33.9/23.6	421	252	3.5/3.4	380	0	18.4	24	B	7	
HBV related DCLD/PHT/Advanced HCC/palliation Chemotherapy	Mr Chinnaswami	50	0	14-Nov-08	47191/08	5000	FALSE		FALSE	TRUE	FALSE	1 year	FALSE	0			FALSE	FALSE	TRUE	TRUE	1	0		TRUE	FALSE	9.3	7600	P52L30E09	234000	32	15/15	1.0	176	33	0.9	1.20/0.77	92	42	3.4/3.8	121	-1	450	6	A	5	1.4x1
DCLD/PHD/ethanol related/HCC right lobe/post RFA	Mr Krishnamurthi	85	0	25-Nov-08	48482/08	5000	TRUE	6 months	FALSE	FALSE	FALSE		FALSE	0			TRUE	TRUE	TRUE	TRUE	1	0	0	FALSE	FALSE	9.5	4100	P69L29E10	103000	29.4	15/15	1.0	118	25.7	0.8	2.7/1.53	100	79	3.5/4.7	422	-1	598	8	A	9	3x3
HBV related DCLD/PHT/HCC 6&7 child B/resection of segment 6&7	Mr Powee	55	0	18-Aug-08	36428/08	25000	FALSE		FALSE	TRUE	TRUE	3 months	FALSE	0			FALSE	TRUE	FALSE	TRUE	1	0		TRUE	FALSE	12	11000	P77L13E10	210000	37	15/16	1.1	77	14	1.1	3.3/2.4	84	32	2.9/4.5	244	0	64.89	13	B		8x6.5
HCV related DCLD/PHT/Advanced HCC/PVT/transient chemotherapy	Mr Nataranjan	58	0	08-Nov-10	39732/10	8000	FALSE		FALSE	FALSE	FALSE		FALSE	0			FALSE	FALSE	FALSE	FALSE				FALSE	TRUE	13.8	6800	P67L28E05	179000	43.8	15/14	1	153	26.2	0.78	1.26/0.8	56	51	4.0/2.7	240	-1	206.7	6	A	8	
HCV related DCLD/PHT/HCC right lobe	Mr Dakshinamurthy	61	0	25-Mar-09	10108/09	3000	FALSE		FALSE	FALSE	FALSE		FALSE	0			FALSE	FALSE	FALSE	FALSE				FALSE	TRUE	12.7	9300	P60L30E10	127000	39.4	15/17	1.2	71	24	1.3	0.41/0.29	124	68	3.3/4.3	290	0	3.24	11	A	9	6.1x5.6
HCV related DCLD/PHT/Advanced HCC right lobe	Mr Bhaskar	62	0	23-Feb-09	6442/09	3000	FALSE		FALSE	TRUE	FALSE	2 months	FALSE	1	15	180	FALSE	FALSE	TRUE	TRUE	1	0	0	FALSE	TRUE	12.8	9100	P69L23E08	196000	41.2	15/14	1.0	95	25	0.7	0.8/0.41	665	119	3.2/3.7	670	0	161	6	A	8	8x6
HCV related DCLD/PHT/HCC/PVT	Mr Mathivanan	42	0	23-Mar-09	11862/09	4000	TRUE	3 months	FALSE	TRUE	FALSE	2 months	FALSE	0			TRUE	TRUE	TRUE	TRUE	1	0	1	FALSE	TRUE	10.2	10500	P74L16E10	290000	32	15/18	1.3	120	11.7	0.7	3.4/2.6	282	227	2.1/5.8	386	-1	4553	11	B	4	
HBV related DCLD/PHT/HCC with PVT left lobe	Mr Murlikrishnan	57	0	09-May-09	15379/09	4000	FALSE		FALSE	TRUE	FALSE	2 months	FALSE	0			TRUE	FALSE	FALSE	TRUE	0	0	0	TRUE	FALSE	11.7	13300	P70L28E02	335000	36.6	15/15	1.0	100	29	1.4	0.4/0.3	26	07	3/4.8	377	-1	1086	10	A	12	
HCV related DCLD/PHT/bilobar HCC with PVT	Mr Parchigam	49	0	30-Jan-09	3346/09	3000	TRUE	1 month	TRUE	TRUE	FALSE	1 month	FALSE	0			FALSE	TRUE	TRUE	TRUE	1	0	1	FALSE	TRUE	13.1	5900	P60L30E10	161000	42.2	15/14	1.0	114	15.7	1.2	3.1/2.2	100	93	3.4/3.6	46	-1	786	12	B	5	
HCV related DCLD/PHT/HCC RFA done	Mrs Pappamal	48	1	18-Feb-09	5743/11	2000	FALSE		FALSE	TRUE	TRUE	3 months	FALSE	0			TRUE	FALSE	FALSE	TRUE	0	0	1	FALSE	FALSE	9.6	10000	P50L40E10	23000	28.8	15/21	1.5	196	19.7	0.5	1.0/0.81	109	69	3/3.5	502	-1	650.56	6	A	14	4x3.8
Ethanol related DCLD/PHT/HCC/PVT(main PV)	Mr Deengaswamy	60	0	24-Dec-08	51650/08	5000	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	2	15	180	FALSE	TRUE	TRUE	TRUE	0	0	1	FALSE	FALSE	12.1	11300	P83L03E08	358000	38	15/21	1.5	127	19.9	0.5	1.6/1.1	85	87	3.3/3.7	761	0	35.8	6	A	6	
HBV related DCLD/PHT/advanced HCC	Mr Gopal	58	0	06-Feb-09	4279/09	3000	FALSE		FALSE	TRUE	FALSE	2 months	FALSE	0			FALSE	FALSE	TRUE	TRUE	0	0		FALSE	FALSE	13	7300	P50L40E10	250000	31	15/14	1.0	70	31	0.5	1.0/0.4	122	134	3.6/4.4	305	-1	1134	6	A	13	6x7
HBV related DCLD/PHT/HCC left lobe	Mr Govindan	56	0	12-Feb-09	1897/09	4000	FALSE		FALSE	TRUE	TRUE	3 months	FALSE	2	10	180	TRUE	FALSE	TRUE	TRUE	1	0	1	TRUE	FALSE	10.8	7000	P60L35E05	347000	34	15/17	1.2	87	31	0.6	1.6/0.54	86	57	2.9/3.2	868	-1	587	6	A	5	12.4x12
Ethanol related DCLD/PHT/advanced HCC	Mr Sampath Kumar	52	0	17-Feb-09	5614/09	3500	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	1	10	270	TRUE	TRUE	TRUE	TRUE	1	0		FALSE	FALSE	8.6	11600	P81L42E07	565000	25	14/15	1.0	150	28	1.0	2.9/1.4	308	95	2.8/4.7	1309	-1	60500	10	B	5	
Ethanol related DCLD/PHT/HCC advanced right lobe of liver	Mr Syed Ebrahim	67	0	23-Dec-08	51563/08	6000	TRUE	4 months	TRUE	TRUE	FALSE	1 month	FALSE	1	15	180	FALSE	TRUE	TRUE	TRUE	1	0	1	FALSE	FALSE	12.7	9100	P72L18E10	344000	40	15/15	1.0	326	28	0.6	7.3/5.0	98	56	3.2/3.4	816	-1	3000	9	B	5	
HCV related DCLD/PHT/Cheld A/HCC right lobe	Mr Anbagham	52	0	22-Sep-08	40558/08	3000	FALSE		FALSE	TRUE	FALSE	1 year	FALSE	2	10	180	FALSE	FALSE	FALSE	TRUE	0	0	1	FALSE	TRUE	12.8	5700	P58L32E10	280000	39.7	15/14	1.0	279	20.6	1.0	1.02/0.97	95	66	4.1/4.1	160	0	20.1	6	A		7.5x6.5
HCV related DCLD/PHT/HCC right lobe	Mr Dhanasekharan	51	0	21-Nov-09	39743/09	10000	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	0			TRUE	FALSE	TRUE	TRUE	1	0		FALSE	TRUE	7.1	1300	P45L45E10	47000	22	15/22	1.8	157	19	1.2	1.7/1.4	57	22	2.3/2.5	205	0	43.1	17	B	5	
HCV related DCLD/PHT/HCC right lobe liver	Mr Manikkam	59	0	04-May-10	15523/10	4500	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	0			TRUE	FALSE	FALSE	FALSE				FALSE	TRUE	10.8	7200	P60L30E10	457000	37.5	15/14	1.0	183	17.7	0.8	1.0/0.95	26	14	4.1/3.7	185	-1	215.71	6	A	11	1.3x1
HCV related DCLD/PHT/Multicentric HCC/old MI	Mr Arulsamy	69	0	20-Mar-10	9992/10	5000	FALSE		FALSE	TRUE	FALSE	15 days	FALSE	0			FALSE	FALSE	FALSE	TRUE	1	0		FALSE	TRUE	12.7	9300	P60L30E10	198000	39.4	15/14	1.0	127	25.5	0.65	0.9/0.6	124	51	3.7/3.2	254	-1	3000	6	A	5	10x8
HCV related DCLD/PHT/HCC left lobe	Mr Arumugam	60	0	09-Dec-10	43398/10	2000	FALSE		FALSE	TRUE	FALSE	3 months	FALSE	2	10	180	TRUE	FALSE	FALSE	TRUE	0	0		FALSE	TRUE	11.4	6900	P65L26E09	126000	35.7	15/14	1.0	112	35.4	1.06	1.2/0.69	105	78	3.6/4.9	501	0	1	8	A	9	3x1
HBV/DCLD/PHT/HCC right lobe	Mrs Parimala	60	1	28-Feb-11	7426/11		TRUE	2 months	FALSE	FALSE	FALSE		FALSE	0			TRUE	FALSE	TRUE	TRUE	1	0	1	TRUE	FALSE	9.7	6900	P76L17E07	223000	29.9	14/19	1.4	123	17.0	0.9	0.74/0.55	66	40	2.3/7.9	210	-1	686	8	A	6	9.2x9
DCLD/PHT/multifocal HCC/BCS	Mrs Chinnapappa	35	1	07-Dec-10	20313/10	2000	FALSE		FALSE	TRUE	FALSE	6 months	FALSE	0			TRUE	FALSE	TRUE	TRUE	0	0	0	FALSE	FALSE	7.5	6900	P65L26E09	113000	39.2	15/14	1.0	119	23.4	0.82	0.71/0.34	57	32	3.8/4.3	327	-1	>1000	6	A	9	6.7x5
HCV related DCLD/PHT/HCC right lobe	Mr Krishnamoorthy	76	0	26-Nov-10	42013/10	2000	TRUE	1 month	FALSE	TRUE	FALSE	2 months	FALSE	0			TRUE	FALSE	TRUE	TRUE	1	1	1	FALSE	TRUE	8.9	13500	P72L20E08	91000	46.1	15/14	1.0	117	47.4	1.12	1.3/0.9	25	29	2.4/3.6	137	-1	768	9	A	8	8x6.4
HBV related DCLD/PHT/Multicentric HCC/SHT/CAHD	Mrs Malliya	56	1	21-Jan-10	2517/10	1500	FALSE		TRUE	FALSE	TRUE		FALSE	0			TRUE	TRUE	FALSE	TRUE	1	0	1	TRUE	FALSE	10.8	2900	P75L16E09	44000	34.1	15/16	1.0	99	32	1.0	1.2/1.0	27	97	2.5/3.3	332	0	12.8	7	A	9	
HCV related DCLD/PHT/Multicentric HCC	Mr Maran	55	0	19-Jul-10	25269/10	3000	FALSE		FALSE	TRUE	FALSE	2 months	FALSE	2	10	180	FALSE	FALSE	FALSE	TRUE	1	1	1	FALSE	TRUE	15.6	13500	P72L20E08	166000	46.1	15/14	1.0	160	31.3	0.77	1.0/0.6	25	29	4.4/2.7	206	-1	592	6	A	7	
Ethanol related DCLD/PHT/HCC	Mr Venkateshaw	45	0	09-Jan-10	1106/10	3000	FALSE		FALSE	TRUE	FALSE	6 months	FALSE	2	15	90	TRUE	FALSE	FALSE	TRUE	0	0	1	FALSE	FALSE	10.9	5900	P72L20E08	106000	32	14/15	1.0	268	19	0.44	1.2/0.8	79	57	2.6/4.7	402	-1	851	6	A	13	7.3x6.1
Ethanol related DCLD/PHT/HCC	Mr Kalyana Sundaram	71	0	30-Dec-10	45656/10	3000	TRUE	6 months	FALSE	FALSE	FALSE		FALSE	2	10	180	TRUE	FALSE	TRUE	FALSE				FALSE	FALSE	4.7	3600	P66L19E10	138000	16.9	14/16	1.2	150	26.3	0.85	7.2/5.6	57	25	3.4/2.8	229	0	4	14	B	9	5.8x5.7
HBV related DCLD/PHT/Advanced HCC/PVTright lobe	Mrs Nasima	30	1	03-Jan-11	271/11		FALSE		FALSE	TRUE	FALSE	1 month	FALSE	0			TRUE	FALSE	TRUE	TRUE	1	0	1	TRUE	FALSE	7.3	4400	P66L20E10	148000	27.3	15/14	1.0	116	19.2	0.47	1.28/0.8	107	32	3.4/4.2	338	-1	300000	6	A	5	13.7x12.8
HBV related DCLD/PHT/Advanced HCC	Mr Ibrahim	47	0	15-Jul-11	24817/10	3000	FALSE		FALSE	TRUE	FALSE	1 month	FALSE	2	10	180	FALSE	FALSE	FALSE	TRUE	0	0	1	TRUE	FALSE	13.3	8500	P71L21E08	394000	44.9	15/14	1.0	112	16.5	0.84	1.0/0.6	111	47	3.6/3.7	218	-1	605000	6	A	8	9.4x6.5
HBV related DCLD/PHT/HCC right lobe	Mr Pedhutu	29	0	13-Aug-09	27327/09	4000	FALSE		FALSE	TRUE	TRUE	2 months	FALSE	0			FALSE	FALSE	FALSE	FALSE				TRUE	FALSE	16	8600	P65L31E04	305000	50.9	15/14	1.0	64	22	0.8	1.2/0.9	20	66	3.4/3,1	2073	0	70.7	6	A	6	20x20
HBV related DCLD/PHT/Bilobar Multicentric HCC	Mrs Tamilarasi	50	1	12-Nov-10	40242/10		FALSE		FALSE	TRUE	TRUE	4 months	FALSE	0			TRUE	FALSE	FALSE	TRUE	1	0	1	TRUE	FALSE	12.3	10400	P75L20E10	352000	42.7	15/15	1.0	73	20	0.8	1.4/0.87	135	135	3.3/3.1	1812	0	12.2	6	A	6	
HCV related DCLD/PHT/HCC	Mr Raman	70	0	16-Nov-10	40785/10		FALSE		FALSE	TRUE	FALSE	6 months	FALSE	2	15	180	TRUE	FALSE	FALSE	TRUE	1	0	1	FALSE	TRUE	11	8200	P69L25E06	392000	34	14/14	1.0	492	30.1	0.9	0.79/0.33	109	33	3.6/3.2	2961	0	0.2	6	A	12	13.5x11.7
HBV related DCLD/PHT/Advanced HCC	Mr Chella Durai	47	0	15-Apr-11	12869/11	3000	TRUE	6 months	FALSE	TRUE	TRUE	1 year	FALSE	0			TRUE	TRUE	TRUE	TRUE	0	0	1	TRUE	FALSE	11.1	6200	P64L24E10	114000	36.5	15/14	1.0	92	19.1	0.7	2.1/1.0	200	183	3.5/3.9	1526	-1	986	6	A	3	
Ethanol related DCLD/PHT/multicentric HCC/child B	Mr Kalliyannan	61	0	03-Jan-11	221/11	3000	FALSE		FALSE	TRUE	TRUE	3 years	FALSE	0			FALSE	FALSE	FALSE	TRUE	1	0	1	FALSE	FALSE	7.5	5300	P71L21E08	85000	27.3	15/15	1.1	95	21	0.6	0.9/0.55	39	27	2.8/3.9	267	0	1.35	6	A	4	5x4
Ethanol related DCLD/PHT/HCC	Mr Pardaram	48	0	07-Nov-09	38016/09	3000	TRUE	1 month	FALSE	TRUE	TRUE	1 month	FALSE	1	10	180	TRUE	TRUE	TRUE	TRUE	1	0	1	FALSE	FALSE	11.2	8600	P80L10E10	133000	36.6	15/17	1.3	80	30.2	0.8	6.1/4.0	128	48	1.9/3.2	1128	0	5.28	14	B	4	
HBV related DCLD/PHT/HCC/locally advanced	Mr Sekhar	44	0	31-Dec-09	44779/09	5000	FALSE		FALSE	TRUE	TRUE	3 months	FALSE	1	10	180	TRUE	FALSE	FALSE	TRUE	1	0	0	TRUE	FALSE	11.9	11900	P74L16E10	430000	40.4	15/16	1.1	125	17.8	0.8	1.5/1.1	54	30	3.5/2.6	928	-1	>3000	7	A	10	11.5x7.2
HBV related DCLD/PHT/HCC right lobe	Mrs Vellachi	48	1	13-Jul-10	24520/10		FALSE		FALSE	TRUE	FALSE	1 month	FALSE	0			TRUE	FALSE	FALSE	TRUE	0	0	0	TRUE	FALSE	11.3	7000	P65L25E10	309000	37.9	15/14	1.0	139	22.3	0.75	0.9/0.5	100	56	2.8/2.5	214	-1	>3000	6	A		10.5x9.5
HCV related DCLD/PHT/HCC right lobe	Mr Mannikam	59	0	19-May-10	2470/10	11000	FALSE		TRUE	TRUE	TRUE	1 month	FALSE	2		occasional	FALSE	TRUE	FALSE	FALSE				FALSE	TRUE	10.8	7200	P60L30E10	457000	32.2	14/26	1.2	183	17.7	0.8	1.0/0.95	26	14	4.1/3.7	185	-1	215.71	6	A	4	

Ethanol related DCLD/PHT/HE/type 2 DM/HCC	Mr Padmanabham	72	0	23-Apr-11	2169/11	5000	TRUE	6 months	FALSE	FALSE	FALSE		FALSE	2	7		TRUE	FALSE	FALSE	FALSE				TRUE	FALSE	12.9	8200	P80L09E11	90000	40.9	14/16	1.1	106	33.94	0.76	1.2/0.8	109	31	2.3/2.4	263	-1	705	6	A		8.5x8.1
HCV related DCLD/PHT/SBP/HCC/PVT	Mr Jhukkanam	48	0	28-Jan-11	225/11	2500	TRUE	3 months	TRUE	TRUE	FALSE	2 months	FALSE	2	13	180	TRUE	TRUE	FALSE	TRUE		0	0	FALSE	TRUE	14	11100	P70L20E10	146000	42.7	14/15	1.0	194	41.2	0.56	3.4/1.9	216	63	3.5/3.4	555	-1	11435	6	A		
HCV related DCLD/PHT/DM/HCC	Mr Ramagle	47	0	11-Jan-11	499/11	12000	FALSE		FALSE	TRUE	FALSE	3 months	FALSE	0			FALSE	FALSE	FALSE	TRUE	1	0	0	FALSE	TRUE	13.9	10100	P65L25E10	281000	43.1	14/22	1.9	95	11.7	0.6	0.8/0.5	36	39	2.9/3.6	431	-1	435.6	7	A	4	
HBV related DCLD/PHT/PVT/PCC	Mr Mohandas	55	0	26-Jan-11	246/11		FALSE		FALSE	FALSE	TRUE		FALSE	0			FALSE	FALSE	FALSE	TRUE	1		1	TRUE	FALSE	10.7	11400	P81L10E09	145000	35.3	15/18	1.3	155	23.82	0.64	1.59/0.99	71	25	2.7/4.7	500		256	6	A		6.9x7.1
HBV related DCLD/PHT/HCC/non alcoholic	Mrs Parimala	60	1	12-Jan-11	319/11		TRUE	1 month	FALSE	FALSE	TRUE		FALSE	0			TRUE	FALSE	FALSE	TRUE	1	0	1	TRUE	FALSE	9.2	6900	P67L20E13	255000	29.1	15/17	26/28	286	10.33	0.63	1.25/0.66	69	37	2.1/4.7	209		12.3	7	B	6	9.2x9
HBsAg DCLD/PHT/HCC	Mr Ragu	60	0		7053/10		TRUE	3 months	TRUE	TRUE	TRUE	2 months	FALSE	0			TRUE	TRUE	FALSE	TRUE	1	0	0	FALSE	FALSE	10.2	7600	P80L20	120000	33	15/18	1.3	176	30.4	0.9	1.0/0.8	56	48	2/3.2	308		392	14	A	7	
HBV related DCLD/PHT/HCC	Mr Mahadevan	56	0		149/09		TRUE	3 months	FALSE	FALSE	TRUE		FALSE	0			FALSE	FALSE	FALSE	TRUE	0	0	0	TRUE	FALSE	9.2	3800	P74L18	85000	32	19	1.3	74	14	0.7	1.4/0.8	63	32	2.1/4.7	190		0.4	6	A	7	8.1x8
HBV related DCLD/PHT/HCC	Mr Sundaraj	42	0		3012/10		FALSE		FALSE	TRUE	TRUE	6 months	FALSE	2	8	180	TRUE	FALSE	FALSE	TRUE	0	0	0	TRUE	FALSE	16.3	7000	P60L30E10	171000	51.3	16	1.2	85	23.3	0.91	1.4/1.0	410	83	3.3/3.8	467		3000	6	B	7	
HCV related DCLD/PHT/PVT/multicentric HCC	Mr Balasubhramaniam	56	0	09-Mar-10	1254/10		TRUE	2 months	FALSE	TRUE	TRUE	1 week	FALSE	0			FALSE	FALSE	FALSE	TRUE	1	0	0	FALSE	TRUE	13.1	6400	P80L13E07	14000	41.1	18	1.3	95	41.1	0.68	5.2/3.7	17	126	2.5/3.9	697		721.67	6	A	9	4.1x3.4